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"Study Of Clinical Profile Of Acne In Post- Adolescent Males and its Association With Metabolic Syndrome And Insulin Resistance "

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I hope my dedication towards medicine stays as strong as his.

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INTRODUCTION

Acne vulgaris is a multifactorial, chronic inflammatory condition of the pilosebaceous units with non-inflammatory (comedones) and inflammatory (papules, pustules, nodules, and cysts) lesions. [1] Acne vulgaris is one of the most common skin conditions worldwide. It normally begins in adolescence and usually ends in the mid-twenties. More than 85% of teenagers and young adults suffer with acne [2]. Because of its ubiquity and influence on patients' social life, it is a critical concern during dermatological consultations. It is one of the most frequent diseases afflicting humans, with significant implications on quality of life (QoL). The influence of acne on QoL in Indian patients is unknown. It affects the skin of the face, neck, upper trunk, and back [2]. Acne vulgaris (AV) affects 9.4% of the world's population and is ranked as the eighth most common illness [3]. Hormonal effects, follicular plugs, follicular hyperkeratinization, increased sebum production, Propionibacterium acnes (P. acnes) colonisation, and inflammation are all involved in the aetiology of AV [4].

Acne pathogenesis begins with increased sebum production, which results in follicular hyperkeratinization. This is followed by a Propionibacterium acnes (recently renamed Cutibacterium acnes) infestation, which results in the production of inflammatory mediators. The typical inflammatory acne seen in the pubertal age range is caused by elevated circulating testosterone levels. Increased insulin levels have also been reported in studies to worsen acne [5].

Acne is caused by the function of lipid metabolism and hormonal activity in sebocyte development. Insulin-like growth factor-1 (IGF-1) is also linked in several aetiologies for excessive sebum production and acne [6]. Previous research has suggested that insulin and growth hormone levels, as well as high IGF-1 levels, may play a role in the development of acne [7,8].

The metabolic syndrome (MS), first described as Syndrome X by Reaven [9], comprises a set of laboratory and physical parameters predisposing the cases to the causation of cardiovascular diseases and diabetes mellitus (Type 2) [10]. Central obesity is considered one of the major constituents of MS. The International Diabetes Federation (IDF) guideline regards it as a defining criterion. Subsequent consensus by the American Heart Association (AHA) and the National Heart, Lung, and Blood Institute (NHLBI) in 2009 recommended

considering central obesity as just one of the criteria. Also, it recommended incorporating ethnicity-specific waist circumference (separately for males and females) [11].

Metabolic Syndrome (MS) is a multiplex syndrome and its prevalence increases with age, racial and ethnic minorities being particularly affected [12]. In the USA, about 25% of the adult population is diagnosed with MS, but in the Middle East region, it's of 15-60% [13]. MS has been reported to be associated with many dermatologic diseases, such as psoriasis and acne vulgaris [14]. Metabolic syndrome causes a group of alterations that increase the risk of developing type II diabetes, arterial hypertension, and cardiovascular diseases. Its prevalence increases with age, and it seen predominantly between 40 and 60 years. [15] Among the etiopathogenic factors, the peripheral resistance to insulin is considered a causative or aggravating factor for acne. [16]

This syndrome arises from insulin resistance and abnormal adipose deposition and function. Insulin/Insulin-like Growth Factor 1 (IGF-1) receptors can be expressed by epidermal keratinocytes, and hyperinsulinaemia may lead to increased proliferation of basal keratinocytes within the follicular sebaceous unit duct, inducing failure of terminal differentiation of follicular corneocytes and thus actively participating in acne pathogenesis [17].

The other parameters include elevated blood pressure, fasting blood sugar and triglyceride levels, reduced high-density lipoproteins. The presence of any three out of the five parameters in an individual is labelled as MS. The pathophysiology of MS is intricately associated with insulin resistance. The tissues like muscles, fat, and other cells, become insensitive to insulin levels in the bloodstream and fail to absorb blood glucose [18]. Central obesity and adipose tissue accumulation play a significant role in developing insulin resistance.

The association of metabolic alterations with other chronic inflammatory skin diseases is already well known, such as lupus erythematosus, psoriasis, rosacea, or hidradenitis suppurativa. [19] Because of the inflammatory and chronic nature of acne, it is probable that acne predisposes to long-term metabolic changes.

Systemic metabolic imbalances are frequently associated with cutaneous symptoms and vice versa [20]. Excess adipose tissue deposition and insulin resistance in MS cause a variety of hormonal abnormalities [21]. Inflammatory markers such as TNF-, IL-17, IL-23, and oxidative stress have been linked to the pathophysiology of MS and acne [22].

It has been proposed that hormonal alterations, particularly during puberty, such as an increase in androgen synthesis and conversion in peripheral tissues, are involved in the aetiology of this illness [23]. Androgens increase the size of the sebaceous glands by increasing sebum production, and they also stimulate keratinocyte proliferation, resulting in acne. Physiologic insulin resistance during puberty induces hyperinsulinemia, which leads to increased androgen synthesis. Acne is also influenced by changes in the levels of insulin-like growth factor (IGF)-1, insulin-like growth factor binding protein (IGFBP)-3, and sex hormone binding globulin (SHBG) [24-26]. Physiological insulin resistance and hyperinsulinemia are responsible for increased free IGF-1 concentrations, androgen production, and decreased IGFBP-3 levels throughout puberty [27]. Insulin-like growth factor 1 induces sebocyte proliferation, raises serum levels of dihydrotestosterone and dehydroepiandrosterone sulphate, and increases mean face sebum excretion rate. [28] Hyperinsulinemia raises epidermal growth factor and transforming growth factor β levels, which raises plasma non-esterified fatty acid levels, producing inflammation and acne. [29] Hyperinsulinemia, on the other hand, begins or aggregates a cluster of metabolic disorders as components of metabolic syndrome by raising plasma fatty acid levels [30]. Similarities in the underlying processes of acne and metabolic syndrome development suggest a probable relationship between these two illnesses.

The aggravation of the mammalian target of rapamycin complex 1 (mTORC 1) signalling pathway is another mechanism connecting insulin resistance and acne development. Stimulation of the mTORC 1 signalling pathway may be significantly linked to acne, higher BMI, insulin resistance, and early menarche. [31] Acne is a frequent symptom of polycystic ovarian syndrome, which affects many women.[32] The pathophysiology of polycystic ovarian syndrome is linked to an impaired hypothalamic-pituitary-adrenal axis and ovarian steroidogenesis with insulin resistance. The metabolic syndrome is a component of polycystic ovarian syndrome. [33] However, relatively few research have looked into the link between acne and metabolic syndrome and insulin resistance in post-adolescent men. [30,34,35]

The primary purpose of this study is to look at a possible link between acne and metabolic changes that may indicate the existence or risk of metabolic syndrome (MS). Because of the link between acne and metabolic syndrome, as well as the impact it has on patient health and the efficacy and safety of treatment choices, it is critical that patients receive proper screening as part of normal medical care.

AIMS : To study the clinical profile of acne in post adolescent males and its association with metabolic syndrome and insulin resistance

OBJECTIVES

1. To study the clinical profile and severity of acne
2. To assess the association of metabolic syndrome and insulin resistance with acne in post adolescent male patients

NEED OF STUDY:

The relationship of metabolic syndrome and insulin resistance with acne in post adolescent males has not been studied extensively, hence this study was undertaken to find the correlation between the same.

REVIEW OF LITERATURE

Epidemiology

Despite the fact that this condition is mostly an adolescent condition, studies show that the age distribution of acne is broadening in both sexes, but especially in women over the age of forty.[36] Previous research in the South Indian population found a male majority [37], but Raghavan JS et al [38] found a female preponderance. This demonstrated that adult acne can either continue from adolescence or appear late in life. Acne was chronic from adolescence in the majority of patients (73.2%) in the study done by Khunger and Kumar [39], but Goulden et al [40] observed that 82% of the study group had persistent acne. Acne, for the most part, appears throughout adolescence and remains into maturity. Historically, there was significant dispute over the role of nutrition in acne control.

Cordain et al. hypothesised that high glycemic diets may have a role in the high prevalence of acne in Western countries. [41] Milk and dairy products were thought to include hormones and bioactive compounds that might worsen acne. According to Sardana et al's study, the majority of acne vulgaris patients' symptoms deteriorated after climate change, particularly during the summer. [42] In their investigation, Khunger and Kumar found that the summer season aggravated 36.7% of patients. [39]

Pathophysiology

Model of Polycystic Ovary Syndrome

The United States National Institutes of Health (NIH) defined Polycystic Ovary (or Ovarian) Syndrome (PCOS) in 1990 as a syndrome that should include (in order of their importance): 1. hyperandrogenemia and/or hyperandrogenism; 2.oligo-ovulation; and 3.exclusion of other known disorders that could cause hyperandrogenism.

This study was clear in recognising PCOS as an androgen excess condition with ovarian implications. Clinical hyperandrogenism has often been regarded as hirsutism under the NIH/NICHD criteria, because more than 70% of hirsute women are hyperandrogenemic. As a result, three primary phenotypes were first identified: 1.women with hyperandrogenemia, hirsutism, and oligo-ovulation; 2.women with oligo-ovulation and hirsutism; and 3.women

with oligo-ovulation and hyperandrogenemia. The appearance of polycystic ovaries by ultrasonography was indicative, but not definitive, of PCOS, according to the NIH/NICHD criteria. The European Society for Human Reproduction and Embryology and the American Society for Reproductive Medicine formed a new agreement in Rotterdam in year 2003, defining the syndrome as the presence of at least two of the following three features: 1. clinical and/or biochemical hyperandrogenism; 2. polycystic ovaries on ultrasonography; 3. oligo- and/or anovulation.

The Rotterdam criteria have extended the pool of possible PCOS patients by creating two additional phenotypes: patients with polycystic ovaries, hirsutism, and/or hyperandrogenemia but normal ovulation and women with polycystic ovaries and irregular ovulation but no indication of androgen excess. Finally, in year 2006, the Androgen Excess Society and the Polycystic Ovary Syndrome Society emphasised hyperandrogenism, implying that it would be an essential condition for the syndrome's diagnosis. Even though the classification of PCOS is still contested, it is the most common endocrine condition associated with acne. It affects about 15-20% of infertile women. Furthermore, PCOS is an excellent illustration of the coexistence of insulin resistance, hyperandrogenism, and hyperinsulinemia. Indeed, insulin resistance is a well-known etiopathogenetic component in females with acne and PCOS. In PCOS, the insulin receptor is both genetically and physiologically normal. Insulin resistance in PCOS is caused by a post-receptor malfunction in insulin signalling, which has been linked to reduced insulin-stimulated insulin Receptor Substrate-1 (IRS-1) activation and decreased GLUT 4 expression. Although insulin resistance is thought to be the cause of hyperandrogenism in PCOS, this mechanism does not explain the hyperandrogenism seen in women with the condition who do not have insulin resistance and/or excess adiposity. Inflammation may be the common thread in the development of insulin resistance associated with PCOS or superimposed excess adiposity. This idea suggests that inflammation may be capable of directly causing hyperandrogenism in PCOS. TNF- alpha's capacity to promote serine phosphorylation makes it an excellent option for beginning these molecular processes in PCOS. Furthermore, while debating the definition of PCOS and the validity of the criteria proposed for its diagnosis, some authors noted that the presence of polycystic ovaries in women who are otherwise not hirsute and have normal ovulation can be associated with the presence of features resembling those seen in PCOS patients. Mild elevations in circulating LH, androgen, and insulin levels, insulin resistance assessed using the homeostatic assessment (HOMA-IR) calculation or the insulin tolerance test, and the LH, 17-

hydroxyprogesterone, and testosterone response to acute long-acting GnRH-analog stimulation are all characteristics of this syndrome. There is some evidence that hyperandrogenemic ovulatory women with and without polycystic ovaries had similar androgen levels and LH/FSH ratios, despite the fact that the former had higher fasting insulin levels, lower glucose-insulin ratios, and a higher 17-hydroxyprogesterone response to leuprolide. These findings indicate that hyperandrogenemic ovulatory women with polycystic ovaries, whether hirsute or not, have minor insulin resistance and mild ovarian dysfunction, but substantially less than women with anovulatory PCOS. Other researchers discovered that fasting and glucose-stimulated insulin and glucose levels, as well as gonadotropin levels, were changed in non-hyperandrogenic women with polycystic ovaries and in PCOS patients. Menstrual irregularity was related with significantly higher serum fasting and stimulated insulin levels in both groups, regardless of androgens or degree of obesity. Finally, PCOS exemplifies the complexities of the interplay between androgens and insulin/IGF-1 and can be utilised as a model of the complicated connection between the immunological and endocrine systems.

It has been demonstrated that metabolic syndrome is an intrinsic component of polycystic ovarian syndrome (PCOS), a prevalent endocrine condition in females related with the production of acne lesions; this syndrome is often characterised by hyperandrogenism, peripheral insulin resistance, and obesity. [43]

1.1 Insulin-like Growth Factors (IGFs) and Growth Hormone (GH) in Acne

The pituitary gland secretes Growth Hormone, which works on the liver and peripheral organs to boost the creation of IGFs (Insulin-like Growth Factors). They were previously known as somatomedins. Growth hormone is secreted in periodic spurts, whereas IGF-1 is generally steady. IGF comes in two varieties: IGF-1 (the most common) and IGF-2. Adolescence is the peak period for growth hormone release. Furthermore, the maximum blood levels of IGF-1 are obtained throughout adolescence. Furthermore, IGF-1 can be generated locally inside the skin, where it can interact with sebaceous gland receptors to induce growth. IGF-1 effects in various tissues can be mediated by androgens, and it has been postulated that androgens may also impact IGF-1 activity in the sebaceous gland. Sebocytes have growth factor receptors such as Epidermal Growth Factor (EGF) and IGF-1. IGF-1's cell

membrane receptor mediates all of its recognised actions. The location of the IGF-1 receptor in normal and diseased tissue gives important information about its function in vivo.

Hodah et al. discovered that the IGF-1 receptor was expressed not only in the epidermis but also in a number of skin appendages. [44] IGF-1 immunoreactivity was observed in the outer roots heath, hair matrix cells, sebaceous gland, eccrine sweat duct, and myoepithelial cells of the eccrine sweat gland secretory part. IGF-1 receptor expression on the cell surface was found mostly in undifferentiated epithelial cells in both the epidermis and skin appendages. The expression of IGF-1 receptors by undifferentiated epithelial cells in normal epidermis, hyperplastic epidermis, and the pilosebaceous unit was predominantly concurrent with proliferating or cyclig cell populations, as measured by Ki-67 nuclear protein expression. Ligand-mediated activation of the IGF-1 receptor is required for cutaneous epithelial cell proliferation in response to other mitogens such as EGF, basic-fibroblast growth factor (bFGF), or Keratinocyte Growth Factor (KGF), and restricted expression of IGF-1 receptors to relatively undifferentiated epithelial cells could explain compartmentalised proliferation. IGF-1 receptor positivity is restricted to the basal layer of the outer root sheath and the germinative layer of the sebaceous gland in pilosebaceous epithelia, whereas EGF receptor immunoreactivity is found in all cells of the outer root sheath and sebaceous gland. The presence of IGF-1 receptor expression in sweat duct epithelium as well as myoepithelial cells, which are metabolically active but mitotically inert, suggests that IGF-1 receptor expression in the skin is not limited to structures engaged in cell replication. IGF-1 is not just a mitogenic agent, but it also regulates the synthetic activity of many different cells. Sex steroids have a well-established effect on the folliculo-sebaceous unit, and multiple lines of evidence relate IGF-1 to sex hormones. There is mounting evidence that IGF-1 has a role in acne. Recent research suggests a link between IGF-1 serum levels and the severity of acne in women [45,46]. In both men and women, IGF-1 serum levels correlate closely with the quantity of face sebum. IGF-1 stimulates keratinocyte proliferation in vitro and in vivo in the skin, as well as lipid synthesis in human sebocytes.

IGF-1 and IGF1-R were shown to be overexpressed in acne lesions relative to healthy skin as this was demonstrated by Isard et al. [47] They discovered that Propionibacterium acnes promotes IGF-1 secretion and induces IGF-1 and IGF-1R expression in keratinocytes. [47] Furthermore, they discovered that IGF-1 and IGF-1R overexpression in acne lesions was linked to an increase in Ki-67 and filaggrin expression in the epidermis, demonstrating that the IGF-1/IGF-1 R system is involved in the control of keratinocyte proliferation and

differentiation. [47] As a result, acne has lately been proposed to be an IGF-1-mediated illness. IGF-1 synthesis activates IGF-1R, which is predominantly found in the basal layer of the epidermis, causing keratinocyte proliferation and an increase in filaggrin expression via a paracrine route. Furthermore, the promotion of lipogenesis and the generation of androgens by IGF-1 enhances acne lesion development. Similarly to growth hormone and IGF1, the level of dehydroepiandrosterone sulphate (DHEAS), the primary adrenal androgen precursor, increases progressively during puberty. It appears to be an important role in the start of sebum production during the prepubertal phase and maybe beyond. Because IGF-1 and DHEAS have a similar temporal tendency, several scientists postulated a probable link between these two hormones.

Cappel et al. investigated the relationship between IGF-1, DHT, and DHEAS in a group of all women, a group of women with clinical acne, and a group of males with clinical acne.[46] Their research backs up previous results showing IGF-1 levels are greater in adult women with acne than in those who do not have acne. [46] Furthermore, they discovered statistically significant relationships between IGF-1 and DHEAS and IGF-1 and DHT in the all-women group, dihydrotestosterone (DHT) and IGF-1 in women with clinical acne, and DHEAS and androstenedione levels in males with clinical acne. [46] Despite these associations, their findings show that IGF-1 and androgens can function independently or dependently on acne lesions counts, depending on the patient group or subgroup. [46] However, IGF-1 appears to have a larger impact in men and women with clinical acne. Furthermore, IGF-1 operated independently of androgens in women with clinical acne. In post-adolescent acne patients, a link between the mean face sebum excretion rate and serum IGF-1 levels has also been observed. [46]

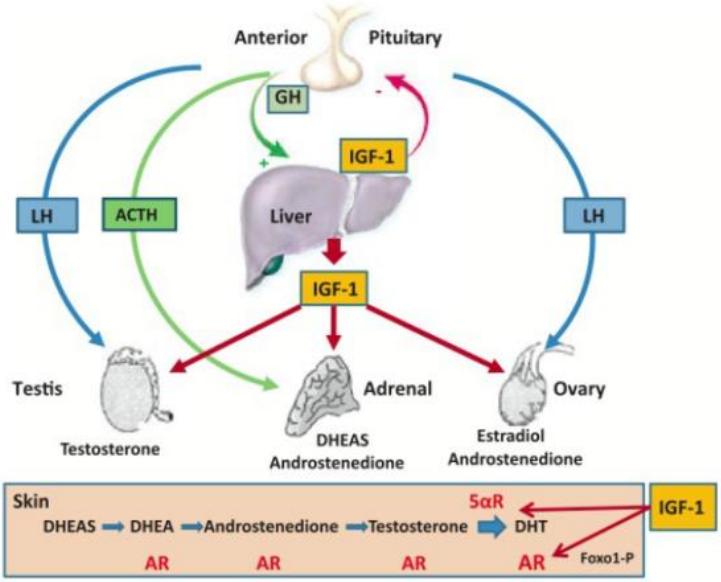

Figure 1. Regulatory network of ACTH, LH, GH, IGF-1 in adrenal and gonadal androgen synthesis and cutaneous intracrine androgen metabolism. (AR=androgen receptor) *[Melnik et al., Experimental Dermatology, 2009;18:833-841]*

1.2 The GH, Insulin, and IGF-1 regulation networks

Sebocyte development and differentiation are influenced differently by GH, insulin, and IGF-1. IGF-1 has a substantial influence on proliferation while having a similar effect on differentiation to insulin. More than 90% of circulating IGFs are coupled to IGFBP-3, the rest to IGFBP-1,-2,-4,-5, and-6, and fewer than 1% circulate as free IGFs. IGF signalling is mediated by the IGF-1 receptor (IGF1R) and the IGF2R. The IGF1R is a tyrosine kinase receptor that may form heterodimers with the insulin receptor (IR). The IGF2R is a scavenger receptor that helps IGF-2 degrade. Insulin attaches to IR mainly, however it can also bind to IGF1R. Furthermore, excessive amounts of insulin, as observed in insulin-resistant individuals, can interact with the IGF-1R.

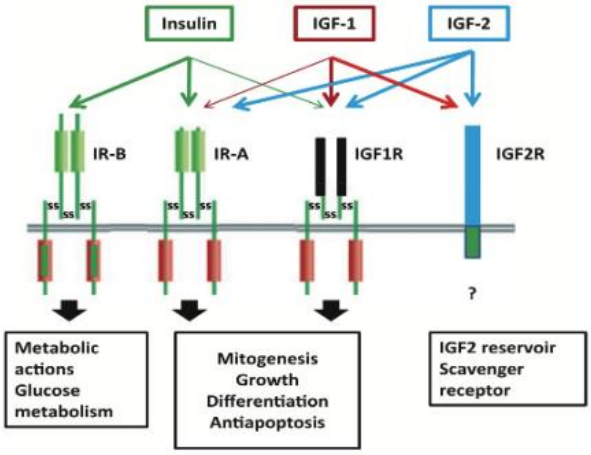

Figure 2. IGF-1, IGF-2 and insulin signal transduction and receptor cross-reactivity inducing mitogenic responses. (IR=insulin receptor) *[Melnik et al., Experimental Dermatology, 2009;18:833-841]*

IGF-1 and IGF-2 bind to their respective receptors but can also bind to IR, explaining the considerable overlap in signal transduction. The Ras-Raf-MAP kinase and the phospho-inositide 3-kinase (PI3K) Akt pathways are activated by IGF1R signals. The IR-B isoform is responsible for the traditional metabolic reactions generated by insulin binding but has a relatively poor affinity for IGFs. The activation of the IR-A isoform by insulin or IGF-2 causes mitogenic reactions similar to those seen with IGF1R. In immortalised human sebaceous gland cell lines SEB-1 and IGF-1, the activation of sterol response element-binding protein-1 boosted lipogenesis (SREBP-1). SREBP-1 predominantly controls fatty acid synthesis genes. Androgens quickly stimulated the expression of SREBP-1 in the hamster ear sebaceous model. Insulin regulates SREBP-1 transcriptionally. IGF-1 has been shown to be important for lipid production and keratinocyte proliferation in immortalised human sebaceous gland cell lines SZ sebocytes. IGF-1 stimulated the PI3K/Akt and MAPK/ERK signal transduction pathways in human SEB-1 sebocytes and promoted the expression of SREBP-1, resulting in enhanced sebaceous lipogenesis. The addition of a particular PI3K inhibitor reduced IGF-1-induced SREBP-1 expression and sebaceous lipogenesis. SREBP-1c is also upregulated in response to insulin signalling. SREBP-1 has been linked to the development of insulin resistance and controls insulin signalling pathway components such as IRS-2 and PI3KR3. All of the newly discovered human genome promoters that bind SREBP-1 and its two related transcription factors, Sp1 and NFY,

constitute a linked regulatory circuit and bind to separate groups of target genes. Members of the Sp-family may be important mediators of insulin-induced gene expression. Insulin controls Sp1's subcellular localization, stability, and transactivation potential [48].

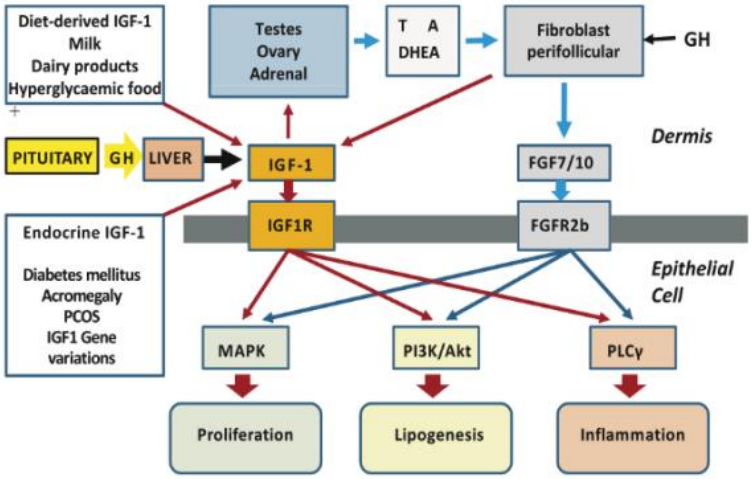

Figure 3. IGF-1 signalling in the pilosebaceous follicle and related interaction with androgen metabolism, androgen-dependent FGF-FGFR2b-signalling, endocrine and nutritional impact on IGF-1 homeostasis. (MAPK=mitogen-activated protein kinase; PI3K=phosphoinositide-3-kinase) *[Melnik et al., Experimental Dermatology, 2009;18:833-841]*

The significance of androgen-dependent FGFR2b signalling in keratinocyte and sebocyte differentiation in acne has recently been explored. IGF1R governs cellular proliferation and, to a lesser extent, differentiation, whereas FGFR2b regulates cellular differentiation. Comedogenesis is defined as an increase in keratinocyte proliferation as well as an increase in keratinocyte differentiation (hyperkeratinization). According to research on human keratinocyte cell culture models, the normalising impact of retinoids on illnesses with hyperkeratinization is mediated via control of differentiation rather than cell proliferation. IGF1R expressed on basal cells and FGFR2b expressed on suprabasal cells regulate classical cellular pathways involved in sebocyte and keratinocyte proliferation and differentiation, as well as activating MAPK- and PI3K-Akt signalling pathways. There is significant qualitative commonality in their recruitment profiles. IGF-1-mediated Androgen Receptor signalling increases the androgen-dependent production of FGF7 and FGF10, the ligands of FGFR2b. In

this manner, IGFR1 signalling has a cooperative impact on FGFR2b signalling. IGF-1 causes the androgen receptor (AR) to transactivate. AR binds to the AR repressive protein Foxo1 in the nucleus. IGF-1 and insulin both activate PI3K, which results in Akt-mediated Foxo1 phosphorylation. Foxo1 that has been phosphorylated exits the AR and translocate from the nucleus to the cytoplasm. IGF-1 signalling, through this pathway, alleviates AR repression, resulting in AR gain-of-function. Thus, IGF-1 has a direct effect on the skin's intracrine androgen regulation and potentiates androgen signalling by inducing 5a-reductase activity and activating AR.

1.3 Insulin resistance

Insulin resistance is defined by impaired cellular glucose absorption and normal or elevated blood insulin levels. The intracellular pool of the insulin-responsive glucose transporter 4 (GLUT4) is significantly decreased in insulin resistance. GLUT4 proteins are retained in recycling endosomes until insulin stimulates the cell to send a high number of GLUT4-containing recycling endosomes to the plasma membrane, allowing for enhanced glucose absorption. In insulin-resistant situations, however, greater than normal insulin levels are necessary to expand the GLUT4 membrane pool for sufficient glucose absorption. Increased insulin levels are normalised when insulin sensitivity improves. Because insulin stimulates hepatic IGF-1 release, metformin's insulin-lowering impact will diminish high blood IGF-1 levels. Insulin also has a transcriptional effect on SREBP-1c. TNFa is a recognised modulator of insulin resistance in obesity-related diabetes syndromes by increasing serine phosphorylation of insulin receptor substrate-1 (IRS-1) in insulin sensitive organs. As a result, the insulin-sensitive glucose transport protein GLUT 4 is expressed less. Insulin Receptor (IR) in PCOS is genetically and functionally normal, as stated in section 1.1. Insulin resistance in PCOS is induced by an insulin signalling post-receptor malfunction, with increased serine phosphorylation suggested as the source of reduced insulin-stimulated IRS-1 activation and GLUT 4 expression. TNF-capacity alpha's to promote serine phosphorylation makes it a good choice for beginning these molecular processes in PCOS.

Acne is usually connected with endocrine illnesses or dietary effects that result in elevated insulin and IGF-1 blood levels. The endocrine system modulates immunological functions, as has been widely established. Indeed, glucocorticoid hormones have significant anti-inflammatory actions on innate immune system cells. TNF alpha-induced insulin resistance is the best studied example of immune-endocrine system interaction. It was described for the

first time in the early 1990s. Proinflammatory cytokines are now recognised to cause resistance in other critical hormone systems, including as glucocorticoids, GH, and IGF-1. Most cell types include intracellular signalling components for both proinflammatory cytokine and IGF receptor-activated pathways, and they are sometimes even shared (ERK-1/2 for both IGF-I and proinflammatory cytokine). This scenario gives rise to the possibility of signal amplification or resistance. TNF-R activated pathways, on the other hand, are well documented to engage in intracellular crosstalk and limit the availability of substrates required by insulin receptor-activated pathways, resulting in resistance. At least two proinflammatory cytokine-activated pathways interact with IGF-IR signalling to impede PI3-K-dependent event induction.

1.4 Insulin and IGF-1's role in Acne Pathogenesis

Acne is linked to excessive sebaceous gland activity. When injected subcutaneously, sebum has been demonstrated to become comedogenic and to produce inflammation. Adrenarche corresponds with an increase in sebum production. Androgens do have a role in expanding the size of the sebaceous gland, promoting sebum production, and encouraging keratinocyte proliferation in the pilosebaceous unit. In addition to androgen levels in the blood, insulin-like growth factor-1 (IGF-1) levels are known to link with the severity of acne in women. Serum IGF-1 levels are also known to be the greatest throughout adolescence, which is when sebum production begins and acne appears. Vora et al. recently discovered a link between the quantity of mean facial sebum excretion (MFSE) and serum IGF-1. Furthermore, this appears to be true in both men and women. Increased IGF-1 may result in increased sebum production. Serum IGF-1 levels were also shown to link with acne lesion numbers in women but not in males. Serum levels of IGF-1, dehydroepiandrosterone sulphate, dihydrotestosterone, acne lesion counts, and face sebum production rate have all been linked to acne. 5 α-reductase, adrenal and gonadal androgen production, androgen receptor signal transmission, sebocyte proliferation, and lipogenesis are all stimulated by IGF-1. In women with acne, the number of total acne lesions, inflammatory lesions, and serum levels of dihydrotestosterone (DHT) and dehydroepiandrosterone sulphate (DHEAS) were linked with serum IGF-1 levels. IGF-1 increases the adrenal's sensitivity to ACTH and stimulates the production and activity of critical enzymes in adrenal androgen formation. A significant connection between IGF-1 and DHEAS blood levels has been documented in both healthy prepubertal girls and prepubertal girls with precocious adrenarche. Normal puberty is

characterised by a condition of transitory insulin resistance coupled with an increase in gonadal sex steroid synthesis and adrenal androgens, and serum IGF-1 levels rise and decrease in a way similar to serum DHEAS. IGF-1 treatment of rat and human skin scrotal fibroblast cultures boosted 5a-reductase activity in a dose-dependent manner. Androgen signalling is increased when testosterone is converted to DHT. The activation of 5a-reductase by IGF-1 indicates that IGF-1 plays a significant function as a peripheral amplifier of androgen metabolism in the epidermis.

Acne is a chronic inflammatory skin condition that mostly affects teenage females' faces, shoulders, backs, and chests. Excess sebum production, follicular hyperkeratinization, Propionibacterium acnes colonisation, and inflammation all play important roles in acne aetiology [49,50]. It has been proposed that hormonal alterations, particularly during puberty, such as an increase in androgen synthesis and conversion in peripheral tissues, are involved in the aetiology of this condition [51]. Acne is also influenced by changes in the levels of insulin-like growth factor (IGF)-1, insulin-like growth factor binding protein (IGFBP)-3, and sex hormone binding globulin (SHBG) [52-54]. Physiological insulin resistance and hyperinsulinemia are responsible for increased free IGF-1 concentrations, androgen production, and decreased IGFBP-3 levels throughout puberty [55]. Hyperinsulinemia, on the other hand, begins or aggregates a cluster of metabolic disorders as components of metabolic syndrome by raising plasma fatty acid levels. 8. Similarities in the underlying processes of acne and metabolic syndrome development suggest a probable relationship between these two illnesses. The connection between a poor metabolic profile and acne has already been discussed [30]. It has been demonstrated that metabolic syndrome is an integral component of polycystic ovary syndrome (PCOS), a common endocrine disease in girls associated with the formation of acne lesions; this syndrome is typically characterised by hyperandrogenism, peripheral insulin resistance, and obesity [56]. According to a recent study, young boys with acne had lower insulin sensitivity and metabolic imbalance with higher values of systolic blood pressure, diastolic blood pressure, waist circumference (WC), waist-hip ratio, body mass index (BMI), serum insulin concentrations, basal glucose concentrations, basal and 120-min levels of the oral glucose tolerance test (OGTT), and homeostasis model assessment-insulin resistance (HOMA-IR), as well as lower levels of serum insulin concentration. Furthermore, another study on young boys found that males with post-adolescent acne frequently had insulin resistance, which was strongly connected with the severity of the condition. They did, however, observe that the frequency of metabolic syndrome was equal

between acne patients and those without acne lesions [30]. The findings of investigations on the link between poor metabolic profiles and acne were inconsistent.

According to a recent study, young boys with acne had lower insulin sensitivity and metabolic imbalance with higher values of systolic blood pressure, diastolic blood pressure, body mass index (BMI), waist-hip ratio, waist circumference (WC), basal and 120-min levels of the oral glucose tolerance test (OGTT), serum insulin concentrations, basal glucose concentrations, and homeostasis model assessment-insulin resistance (HOMA-IR), as well as lower levels of serum insulin concentration. Furthermore, another study on young boys found that males with post-adolescent acne frequently had insulin resistance, which was strongly connected with the severity of the condition. They did, however, observe that the frequency of metabolic syndrome was equal across acne patients and those without acne lesions. [30]

When compared to adult and pre-pubertal age, the response to a glucose load is enhanced throughout puberty and adolescence, but insulin sensitivity is decreased physiologically. Insulin is a hormone that operates at various levels along the axis that regulates sex hormones. It promotes the production of androgens in the gonads and the synthesis of androgenic precursors in the adrenal glands, as well as the release of LH and FSH by the pituitary gland. Finally, it inhibits the formation of Sex Hormone Binding Globulin in the liver (SHBG). It was also shown that insulin may act directly on sebum production and increase the effects of IGF-1 in the skin by blocking the formation of its binding protein (IGF bindingprotein-1, IGFBP- 1). As a result, disruptions in insulin metabolism may lead to the development of acne. Treatment-resistant acne is not uncommon in clinical practise. We identified two categories of patients whose acne does not appear to be caused largely by an androgen hormone imbalance. Female patients with chronic acne or late-onset acne are included in the first category. Androgen levels in these individuals' blood are typically normal, and their treatment-resistant acne does not appear to be due to hyperandrogenism. Male patients with treatment-resistant acne make up the second category of patients. We chose to focus on the latter group of patients since the association between acne and insulin resistance in men has received little investigation. Based on recent results demonstrating the importance of insulin and IGF-1 in the pathogenesis of acne vulgaris, we hypothesised that IGF-1 and insulin might play a crucial role in the development of treatment resistance in these people.

Nada et al. (2021) conducted a randomised case control study on 52 post-adolescent male acne sufferers and 52 individuals (age and gender matched) as controls. They investigated the prevalence of MetS (metabolic syndrome) in post-adolescent male acne vulgaris [AV] patients (aged >20 years) and the relationship between MetS and the severity of AV in these individuals. MetS prevalence was observed to be statistically significantly greater in AV patients (19.2%) compared to controls (5.8%). (x2=4.37, p =0.037). The odds ratio was 3.9 (1.003 to 15.07), p=0.049, and there was a statistically significant relationship between AV and the chance of getting MetS. The severity of AV and MetS prevalence had a statistically negligible relationship. MetS prevalence was greater in AV patients than in controls, and it was more prevalent in individuals with severe acne, they concluded. A statistically significant relationship existed between AV and the likelihood of having MetS. [57]

Shariatpanahi et al. (2020) studied the prevalence of metabolic syndrome and its components in teenage girls with acne against a control group in a cross-sectional research of 105 adolescent girls aged 12-18 years. They discovered that the prevalence of metabolic syndrome was 18.2% and 14% in individuals with and without acne, respectively. In teenage girls, metabolic syndrome was not associated with acne (P = 0.561). Furthermore, the mean BMI (P = 0.89), waist circumference (P = 0.62), systolic and diastolic blood pressures (P = 0.57 and 0.62, respectively), fasting blood sugar (P = 0.59), total cholesterol, and low-density lipoprotein cholesterol levels were comparable (P > 0.05). Furthermore, triglyceride levels were considerably lower in the acne group (P = 0.028), whereas high-density lipoprotein cholesterol levels were greater (P = 0.02). However, the logistic regression findings revealed that none of the tested lipids were linked to acne. Their findings showed that metabolic syndrome and its components (indicating metabolic imbalance) were not associated with acne in teenage females. [58]

Chandak et al. (2022) did cross-sectional research with 65 acne vulgaris patients and 65 age and sex-matched controls to look for any probable link between Acne Vulgaris and Metabolic Syndrome. On clinical assessment, they discovered that grade 2 acne was the most common. Among the patients, they found an increased incidence of aberrant waist circumference, triglyceride, HDL, and fasting blood glucose (p0.05). As a result, the case group had a higher prevalence of MetS (p=0.011). When we compared the mean values of the data, we discovered a substantial difference in waist circumference and HDL levels. The case group had an increased mean value of waist circumference, while the control group had an increased mean value of HDL (p0.05). They concluded that people with acne vulgaris are

more likely to acquire MetS. As a result, a thorough investigation of clinical, anthropometric, and biochemical characteristics that may contribute to the development of MetS is required. [59]

Thappa DM and Rashmi Kumari discussed the significance of insulin resistance and nutrition in acne. They emphasised that milk intake and hyperglycemic diets can increase insulin and IGF1mediated PI3K Akt activation, which can worsen acne by increasing sebaceous lipogenesis, sebocyte, and keratinocyte proliferation. The presence of acne as part of numerous syndromes adds to the evidence for a link between IGF1 and acne. [60]

Nagpal et al. (2016) conducted a cross-sectional research with 100 male acne sufferers and 100 age-matched male controls. They looked at the frequency of metabolic syndrome and insulin resistance in acne patients aged 20 and above. They discovered that the prevalence of insulin resistance was substantially greater in cases (22%) than in controls (11%) (P =.03). The prevalence of metabolic syndrome was comparable in patients (17%) and controls (9%), with a P =.09 difference. The prevalence of insulin resistance and metabolic syndrome was not substantially different across acne severity groups. They concluded that insulin resistance is more frequent in postadolescent male acne sufferers. Resistance to insulin may be a sign of prediabetes, and individuals may develop hyperinsulinemia or type 2 diabetes in the future. These individuals should be monitored for a long period to see if they develop insulin resistance-related diseases. [30]

Munichandrappa et al. (2017) used a homeostasis model evaluation of insulin resistance among 45 cases and 45 controls to compare insulin resistance in acne patients and controls. They discovered no statistically significant difference between patients and controls in fasting insulin levels. However, a slight positive connection (r=0.3, p=0.04) was seen between acne severity and fasting insulin levels. The differences in fasting glucose levels and HOMA-IR values detected between cases and controls were not statistically significant (p=0.05 and p=0.59, respectively). Their research did not indicate that insulin resistance played a significant influence in acne. [61]

The main goal of this study is to investigate a possible relationship between acne and metabolic alterations which can represent risk or presence of metabolic syndrome (MS) especially in post adolescent males and can be diagnosed by routine screening . The paucity of data in the literature prompted us to conduct this study.

MATERIALS AND METHODS

STUDY DESIGN: CROSS SECTIONAL STUDY

PLACE OF STUDY: Department of Dermatology, Santosh Medical College and Hospital, Ghaziabad

STUDY POPULATION: Patients with acne vulgaris attending the outpatients' clinic of Department of Dermatology, Santosh Medical College and Hospital, Ghaziabad were included in the study after their consent.

DURATION OF STUDY: One year

SAMPLE SIZE: 216

ETHICAL CLEARANCE: Clearance from Institutional ethical committee of Santosh medical college and hospital Ghaziabad was obtained prior to conducting this study

INCLUSION CRITERIA

1.Male Patients with acne vulgaris of age ≥20 yrs.

EXCLUSION CRITERIA

1. Patients with history of smoking and alcoholism .
2. Patients with history of Cushings syndrome
3. Patients with history of Acromegaly.
4. Oral isotretinoin therapy within past 1 year.

METHODOLOGY:

A total of 108 post adolescent male patients with acne vulgaris attending the outpatients' clinic of Department of Dermatology, Santosh Medical College And Hospital were included in the study.

Equal number of age matched male controls without acne were enrolled.

Detailed demographic data of all patients was recorded in a preset proforma.

History regarding onset and duration of acne, severity, aggravating factors, medical history, family history and treatment received was taken.

Written informed consent was obtained from all the participants in the study.

Detailed examination of acne will be done under good illumination to assess the number, distribution and type of acne lesions.

Assessment of severity of acne was done using **Global Acne Grading System :** 6 locations were selected on face / chest / upper back.

LOCATION	I. FOREHEAD	II. RIGHT CHEEK	III. LEFT CHEEK	IV. NOSE	V. CHIN	VI. CHEST AND UPPER BACK
FACTOR	2	2	2	1	1	3

Each location is graded on 0-4; with the most severe lesion determining grade for that area:
(0 =No lesions; 1 ≥one comedonc ; 2.≥one papule; 3≥one pustule; 4 .≥one nodule)
Grade X Factor = local score

Global Score = sum of all the local scores

Global score:

0=None

1-18=Mild

19-30=Moderate

31-38=Severe

>39 Very severe

The waist circumference was measured in a horizontal plane, midway between the inferior margin of the ribs and the superior border of the iliac crest and Blood pressure(BP) was measured at the time of examination. Blood pressure was measured at the time of examination in lying down position from right hand.

Laboratory investigations like fasting blood Sugar, fasting insulin, fasting serum triglycerides, high-density lipoprotein cholesterol (HDL-C) were taken after 8 hrs of fasting.

Based on above the metabolic syndrome defined by modified NCEP ATP-III guidelines consists of three or more of the following and was recorded as follows:

1. Fasting plasma glucose ≥100 mg/dl (Modified for Asian men) ,

2. Serum triglycerides ≥150 mg/dl or drug treatment for elevated levels,

3. Serum HDL cholesterol <40 mg/dl or drug treatment for elevated levels ,

4. BP ≥130/85 mmHg or on BP medication or drug treatment for hypertension,

5. Waist circumference>90cm (modified for Asian men).

Insulin levels was estimated with an electrochemiluminescence immune assay done using Roche fully automated analyser e411. The HOMA-IR (Homeostasis Model Assessment–Insulin Resistance) values were calculated using the following formula:

Fasting Insulin (Microunits per Milliliter) × Fasting Glucose (Micograms per Deciliter)/405.

A HOMA-IR value greater than 2.5 is predefined arbitrarily as insulin resistance.

DATA MANAGEMENT AND STATISTICAL ANALYSIS:

STATISTICAL ANALYSIS : A P value of <0.05 was considered to indicate statistical significance. The normality of quantitative data was checked by measures of Kolmogorov-Smirnov test of normality. For normally distributed data mean values of three groups was compared using one way analysis of variance (ANOVA). Analysis will be conducted using R software version 4.0.2

RESULTS

A total of 216 male patients were involved in the study. 108 patients with acne were selected and equal number of age matched controls were selected in this study for comparison of data.

The mean age, weight, height and waist circumference of the cases were 21.52±1.63 years, 67.14±6.27 Kg, 160.81±4.18 cm and 88.14±5.16 cm; and of controls were 22.24±2.15years, 63.40±5.21Kg, 161.27±3.71cm, and 85.49±5.36cm, respectively (p-value 0.24, <0.001, 0.8 and <0.001, respectively). [table 1; Fig. 1-4]

Table-1. Demographic profile comparison in between cases & control

Factor	Cases	Controls	p-value
Age (years)	21.52±1.63	22.24±2.15	0.24
Weight (Kg)	67.14±6.27	63.40±5.21	<0.001
Height (cm)	160.81±4.18	161.27±3.71	0.8
Waist Circumference (cm)	88.14±5.16	85.49±5.36	<0.001

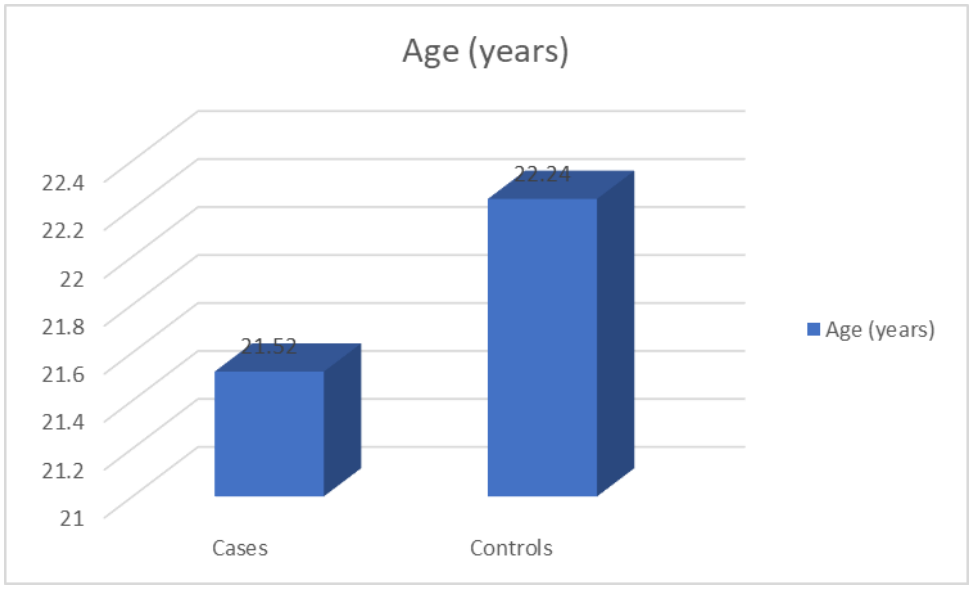

Fig.1: Age wise distribution among cases and control participants.

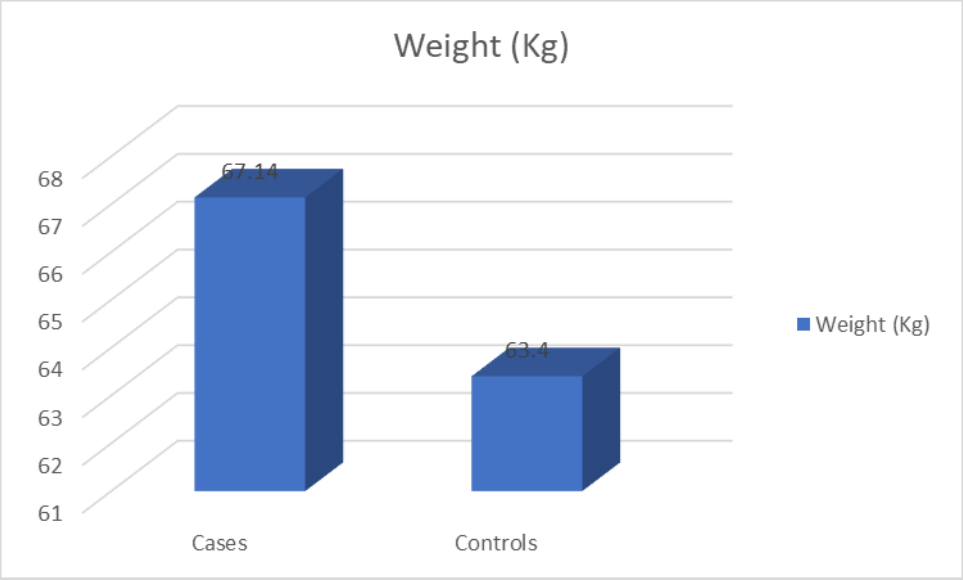

Fig.2: Weight wise distribution among cases and control participants.

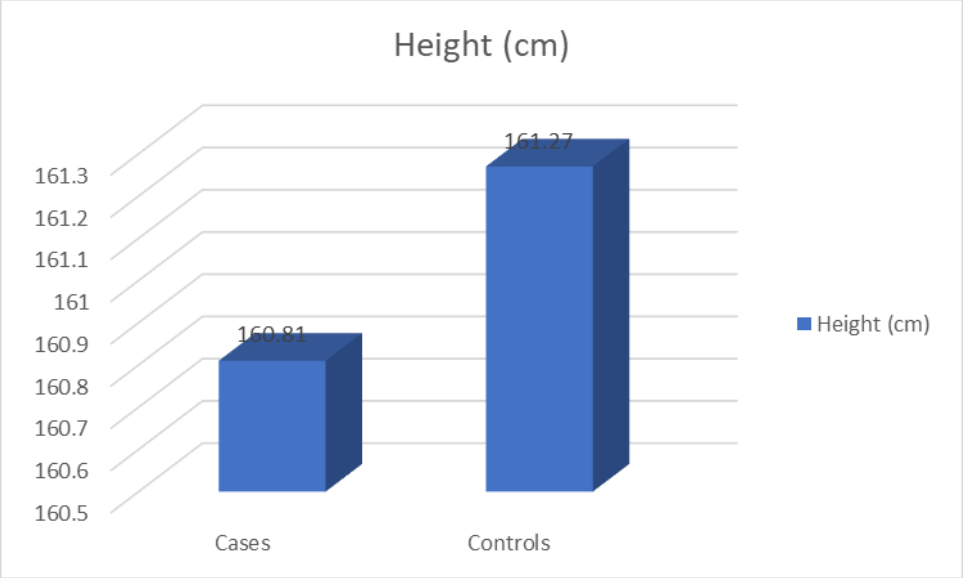

Fig.3: Height wise distribution among cases and control participants.

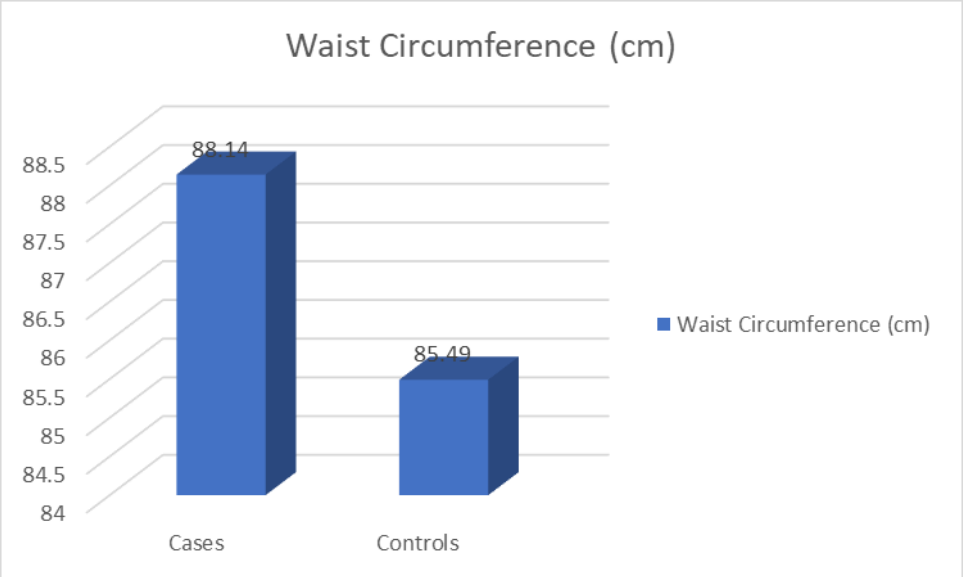

Fig.4: Waist wise distribution among cases and control participants.

Table-2. Study Parameters in both Study Groups

Factor	Cases	Controls	p-value
SBP (mmHg)	128.65±8.13	121.57±8.29	<0.001
DBP (mmHg)	82.01±7.27	74.49±6.39	<0.001
Serum HDL (mg/dl)	46.37±8.52	44.86±8.17	0.097
Serum Triglycerides (mg/dl)	108.14±40.39	98.22±34.08	0.019
Fasting Blood Glucose (mg/dl)	88.33±5.44	81.34±7.03	<0.001
Fasting Plasma Insulin (µIU/ml)	9.56±4.83	8.33±3.07	0.059
HOMA-IR	2.24±1.04	1.84±0.63	0.003
Metabolic Syndrome (%) *	28.48	10.56	<0.001
Insulin Resistance (%) $^{\infty}$	26.35	12.30	0.008

Data are mentioned as Mean ± S.D lest specified otherwise; SBP=systolic blood pressure; DBP=diastolic blood
pressure; HOMA-IR=Homeostasis Model Assessment-Insulin Resistance; HDL-C=high density lipoprotein
cholesterol; *Metabolic syndromes assessed by National Cholesterol Education Program Adult Treatment Panel
III (NCEP-ATPIII); $^{\infty}$ Insulin resistance outlined as HOMA-IR score >2.5.

The mean systolic and diastolic blood pressures of the cases were 128.65±8.13mmHg and 82.01±7.27 mmHg, and were significantly high when compared with controls i.e.

121.57±8.29 mmHg and 74.49±6.39 mmHg, respectively (p<0.001 for both). The mean fasting blood glucose level and HOMA-IR score of the cases were 88.33±5.44 mg/dl and 2.24±1.04, and were significantly higher than they were of controls i.e. 81.34±7.03 mg/dl and 1.84±0.63, respectively (p <0.001 and 0.003, respectively).

The mean serum triglyceride level of the cases (108.00±40.39mg/dl) was significantly higher (p=0.019) than that of controls (98.14±34.08mg/dl). Both the groups were comparable in terms of serum HDL cholesterol levels and fasting plasma insulin concentrations (46.37±8.52mg/dl and 9.56±4.83 µIU/ml in the cases; and 44.86±8.17mg/dl and 8.33±3.07 µIU/ml in controls, p-value 0.097 and 0.059, respectively.

The percentage of metabolic syndrome was 28.48% in the cases and 10.56% of the controls and the difference was statistically significant (p=<0.001). Insulin resistance, defined as HOMA-IR score of more than 2.5, was noticed in 26.35% of the cases and 12.30% of the controls and the difference was also statistically significant (p=0.008). (Table-2)

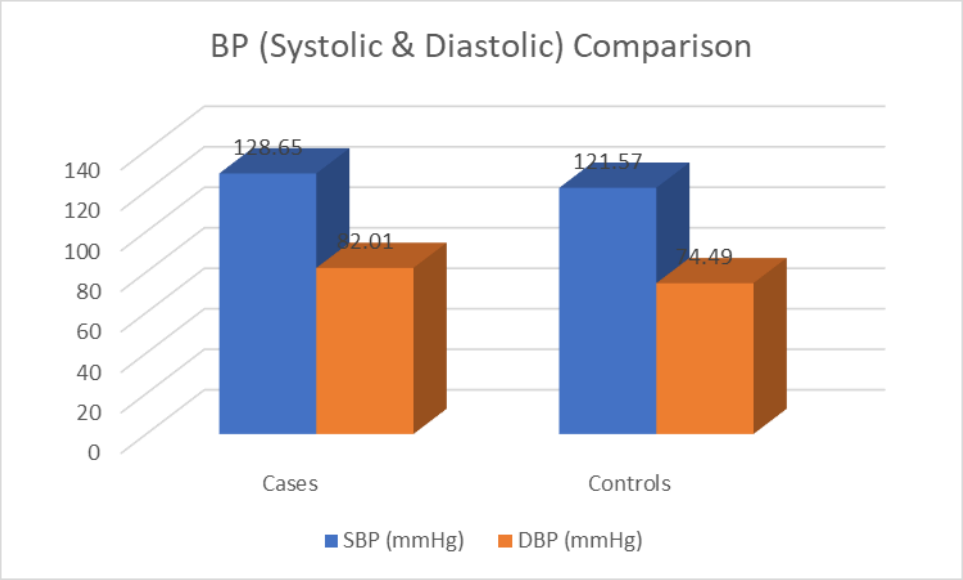

Fig.5: BP (systolic and diastolic)pcomparison among cases and control participants.

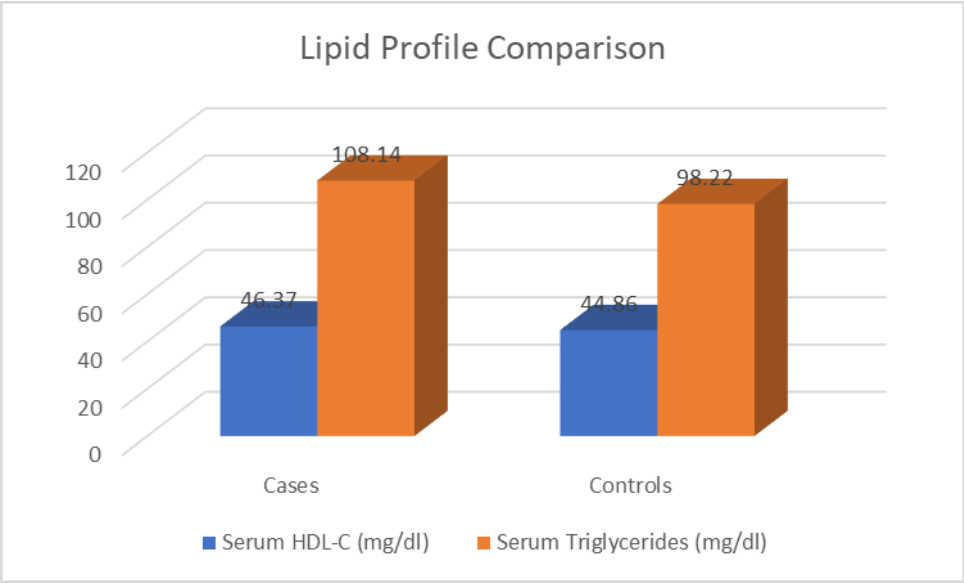

Fig.6: Lipid profile (HDL, Triglyceride) pcomparison among cases and control participants.

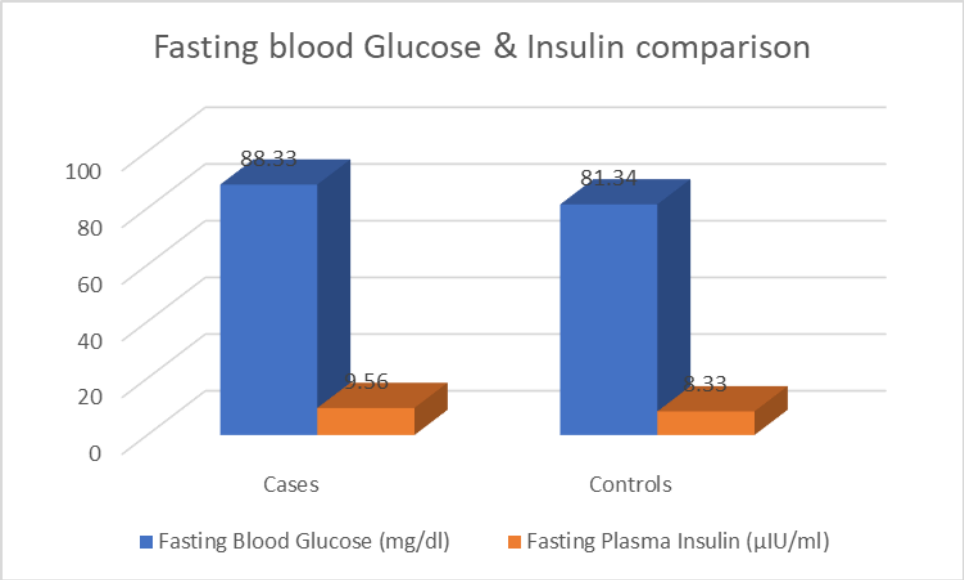

Fig.7: Fasting blood glucose and Insulin comparison among cases and control participants.

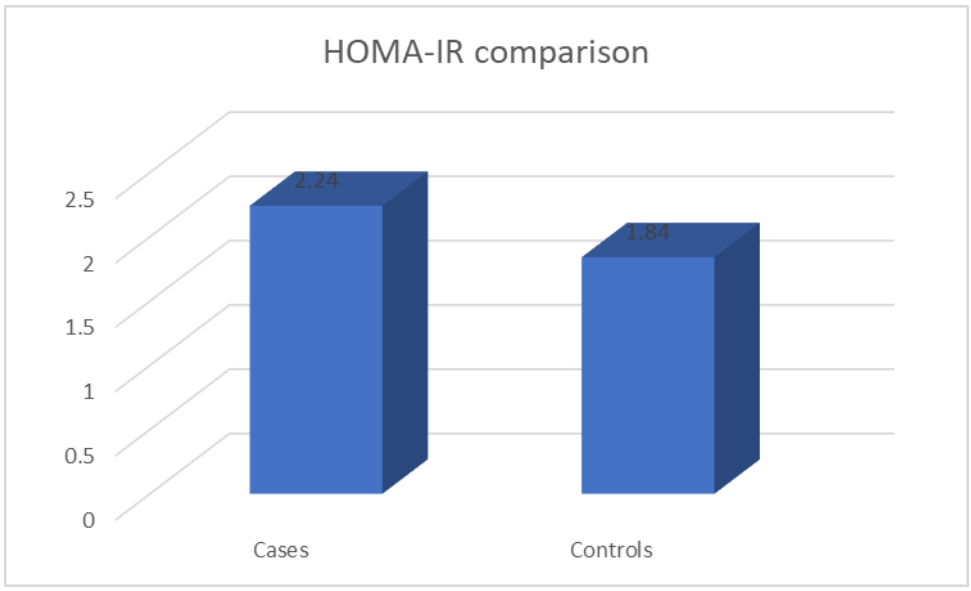

Fig.8: HOMA-IR comparison among cases and control participants.

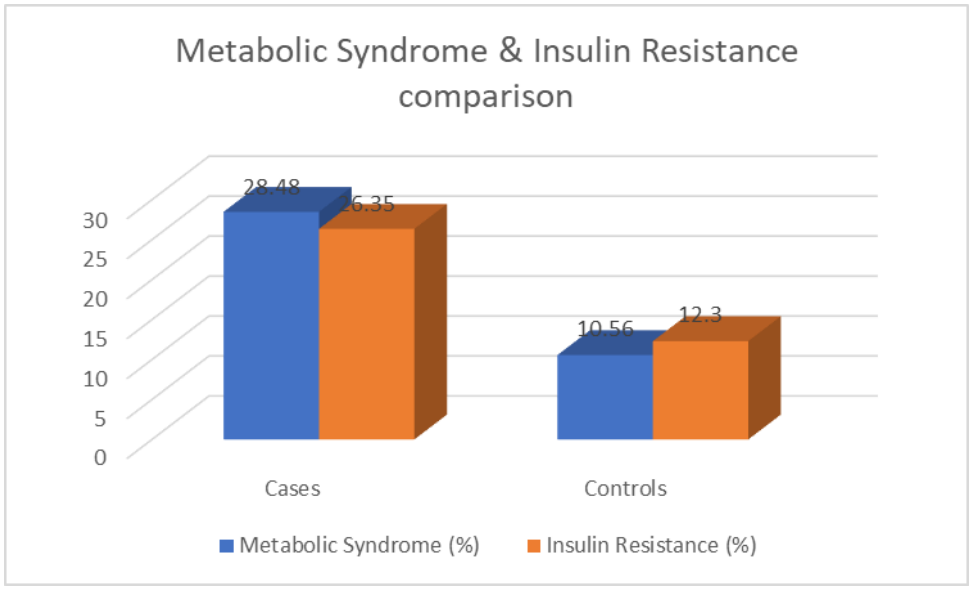

Fig.9: Metabolic syndrome and Insulin resistance comparison among cases and control participants.

Table-3, Study parameters in Four Acne Severity Groups

Parameter	Mild Acne	Moderate Acne	Severe Acne	Very Severe Acne	P value
Age (years)	21.50±1.22	21.25±2.21	22.50±3.51	23.43±3.66	0.05
Weight (Kg)	56.50±4.32	60.80±5.48	65.25±6.68	68.36±6.26	<0.001
Height (cm)	160.75±4.49	161.00±3.91	161.25±4.49	162.47±4.11	0.50
Waist Circumference (cm)	86.5±5.48	85.60±5.31	86.52±4.65	87.24±5.66	0.72

The differences of mean age and weight were significantly different in four groups of acne severity, in mild or moderate acne being the lowest and in very severe acne being the highest (p-value .05 and <.001, respectively). The mean height and waist circumference was not statistically different (p-value .50 and .72, respectively).

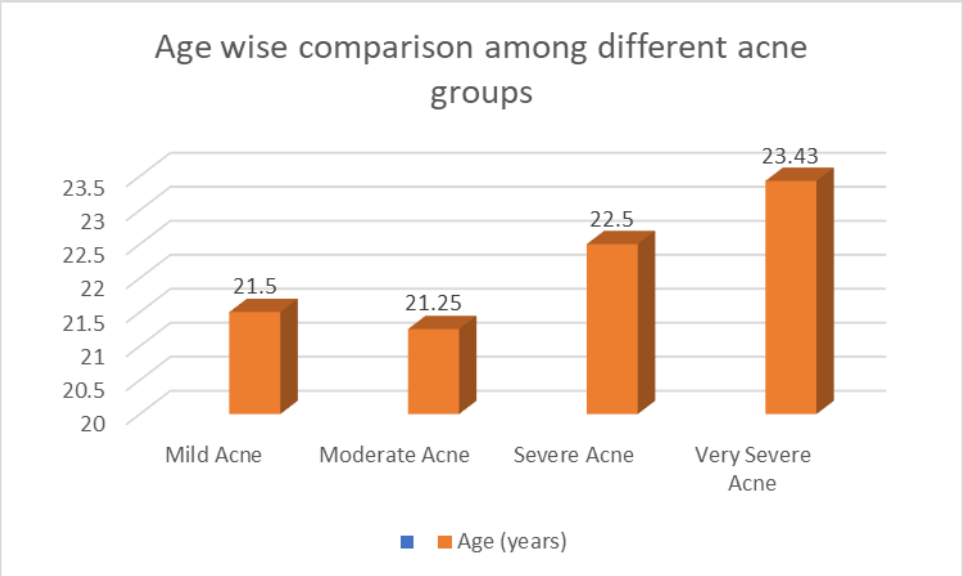

Fig.10: Age wise comparison among different acne severity group participants.

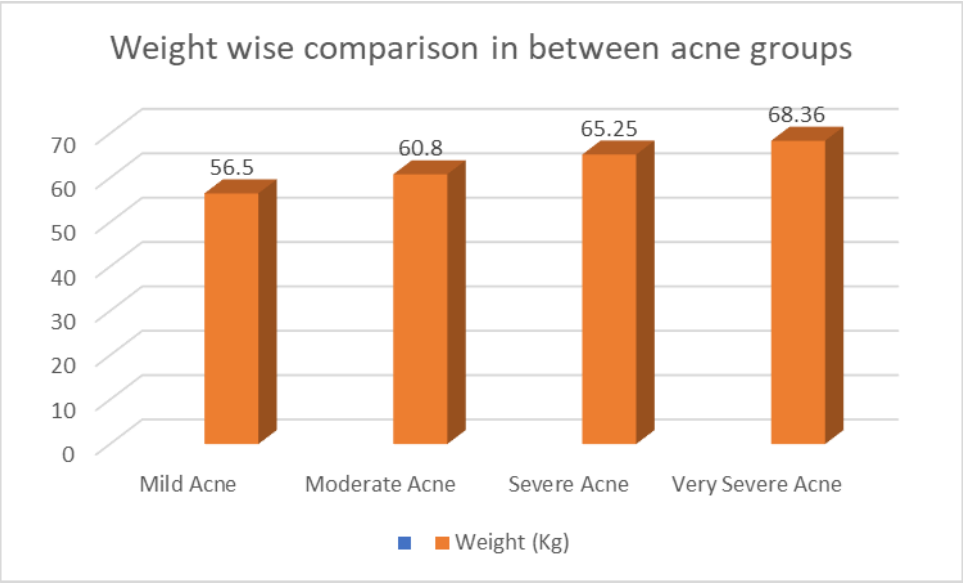

Fig.11: Weight wise comparison among different acne severity group participants.

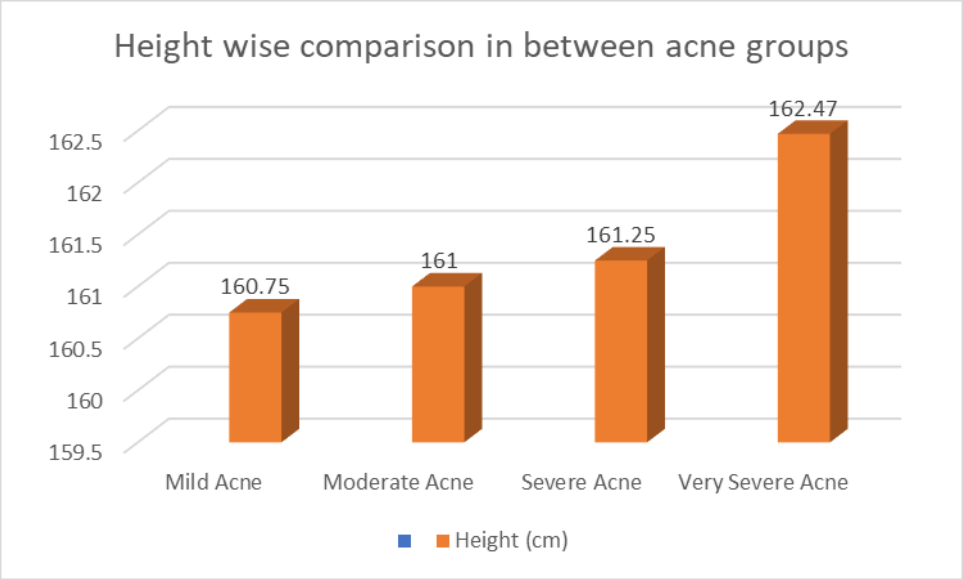

Fig.12: Height wise comparison among different acne severity group participants.

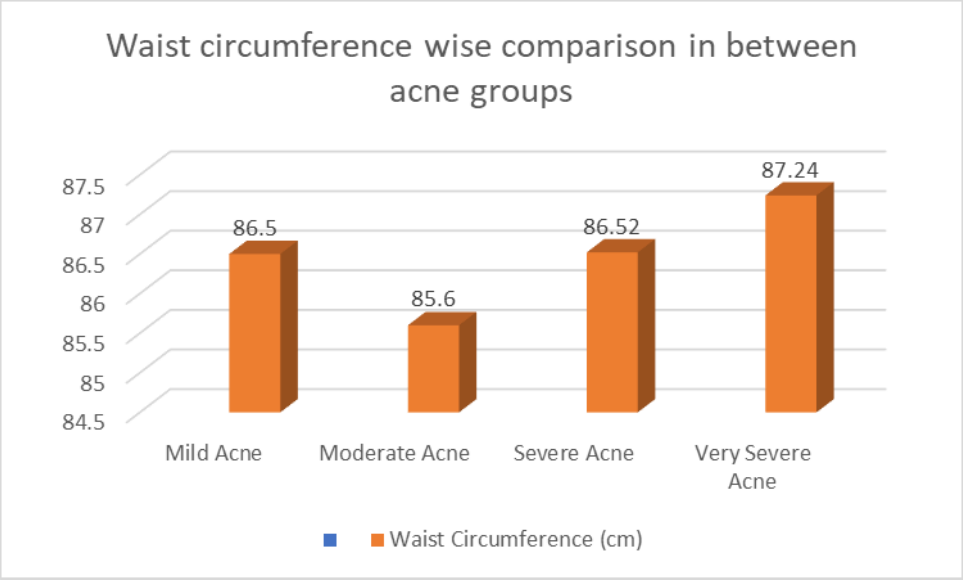

Fig.13: Waist circumference wise comparison among different acne severity group participants.

Table-4, Study parameters in Four Acne Severity Groups

Parameter	**Mild Acne**	**Moderate Acne**	**Severe Acne**	**Very Severe Acne**	**P value**
SBP (mmHg)	125.25±6.1	127.30±7.21	130.40±6.15	133.20±8.45	0.03
DBP (mmHg)	75.84±5.7	77.20±4.9	79.50±6.10	82.40±5.49	0.02
Serum HDL (mg/dl)	45.40±6.7	46.25±7.80	47.5±6.33	46.49±6.44	0.50
Serum Triglycerides (mg/dl)	90.65±42.0	92.65±41.03	91.05±38.39	94.79±40.92	0.90
Fasting Blood Glucose (mg/dl)	90.55±4.00	91.80±4.68	92.90±4.39	90.25±3.72	0.50
Fasting Plasma Insulin (µIU/ml)	9.18±4.07	9.2±4.26	9.09±5.1	10.25±4.7	0.80
HOMA-IR	2.08±1.08	2.30±1.22	2.34±1.03	2.54±1.24	0.40
Metabolic Syndrome (%) *	19	21	28	32	0.02
Insulin Resistance (%)$^{\infty}$	20	26	24	30	0.01

Data are mentioned as Mean ± S.D lest specified otherwise; SBP=systolic blood pressure; DBP=diastolic blood

pressure; HOMA-IR=Homeostasis Model Assessment-Insulin Resistance; HDL-C=high density lipoprotein

cholesterol; *Metabolic syndromes assessed by National Cholesterol Education Program Adult Treatment Panel
III (NCEP-ATPIII); ∞ Insulin resistance was outlined as HOMA-IR score >2.5.

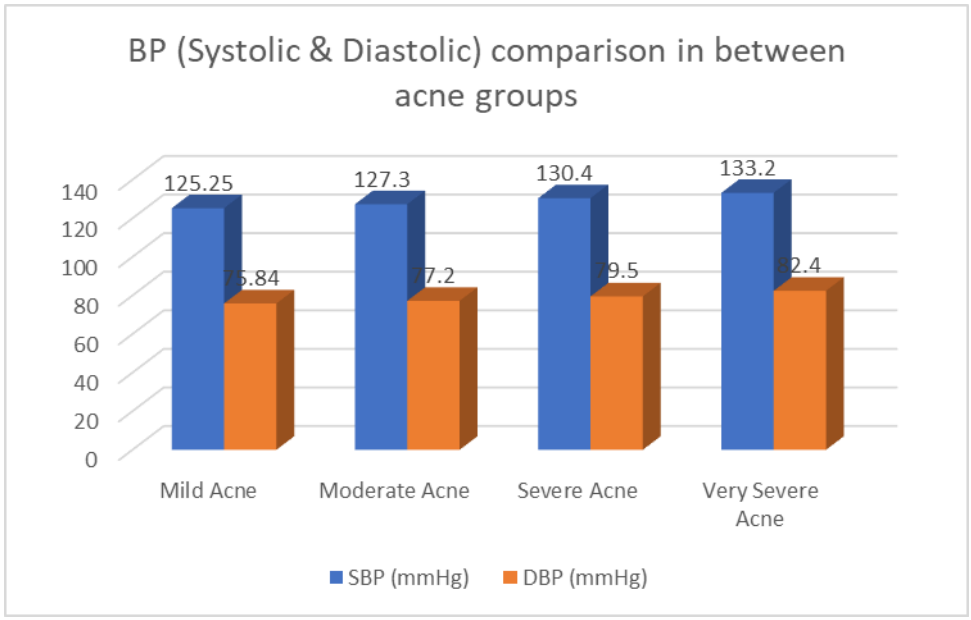

Fig.14: BP (systolic & diastolic) comparison among different acne severity group participants.

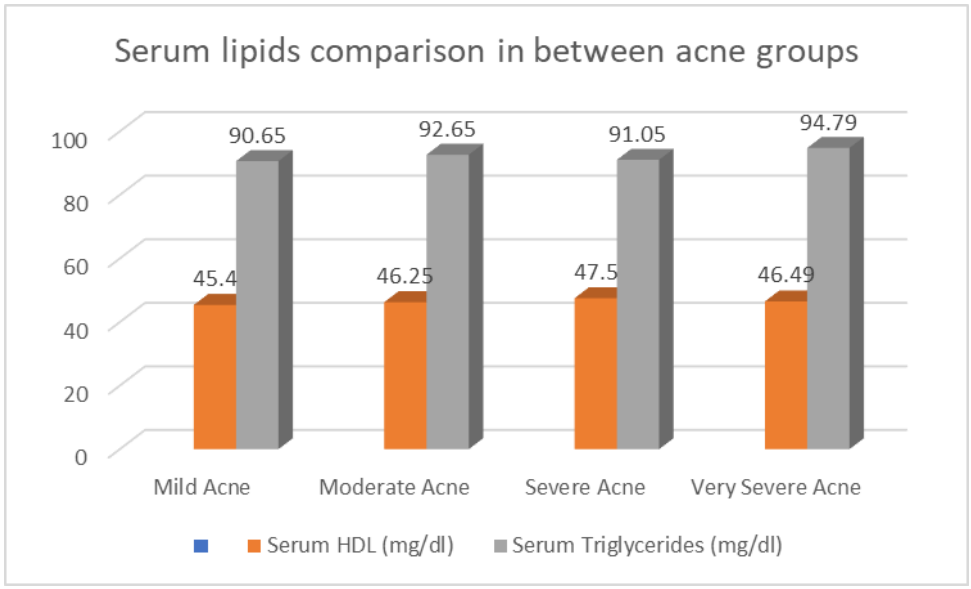

Fig.15: Serum lipids comparison among different acne severity group participants.

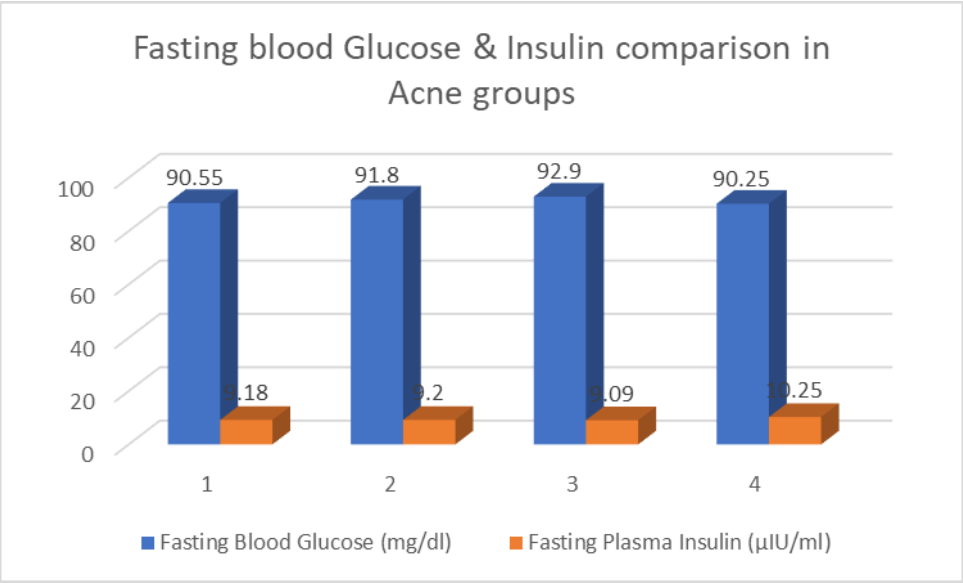

Fig.16: Fasting blood glucose & Insulin comparison among different acne severity group participants.

The difference of systolic and diastolic blood pressure was statistically different in four acne severity groups (p-value .03 and .02, respectively), with systolic blood pressure and diastolic blood pressure being the lowest in mild acne group.

There was no statistically significant difference in serum HDL-Cholesterol level, serum triglycerides level, fasting blood glucose levels, fasting plasma insulin levels and HOMA-IR score among these four groups (p-value >0.05 respectively).

The percentage of metabolic syndrome and insulin resistance was 19% and 20% in mild acne; 21% and 26% in moderate acne; 28% and 24% in severe acne; and 32% and 30% in very severe acne groups, respectively. The differences were statistically significant (p-value .02 and .01 for metabolic syndrome and Insulin resistance, respectively). (Table-4)

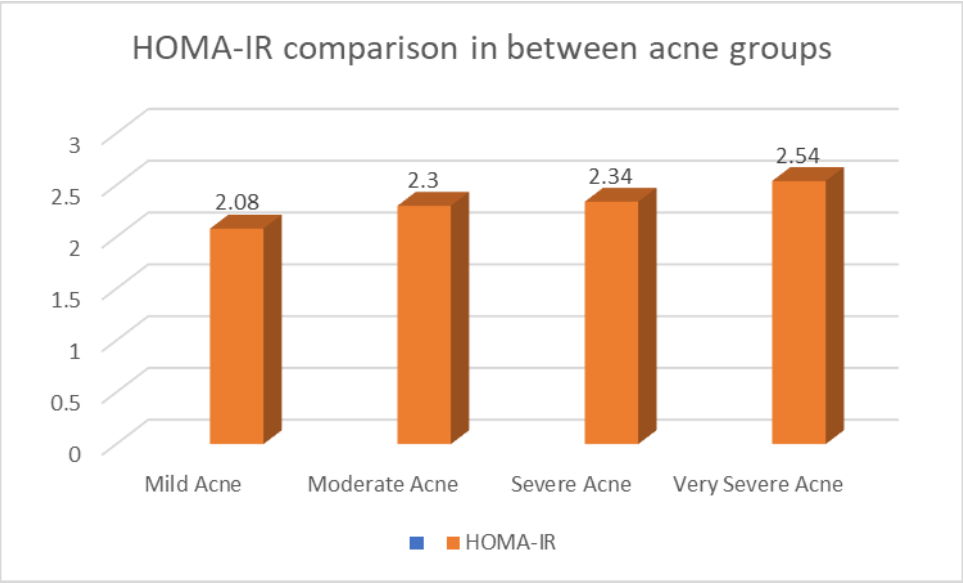

Fig.17: HOMA-IR comparison among different acne severity group participants.

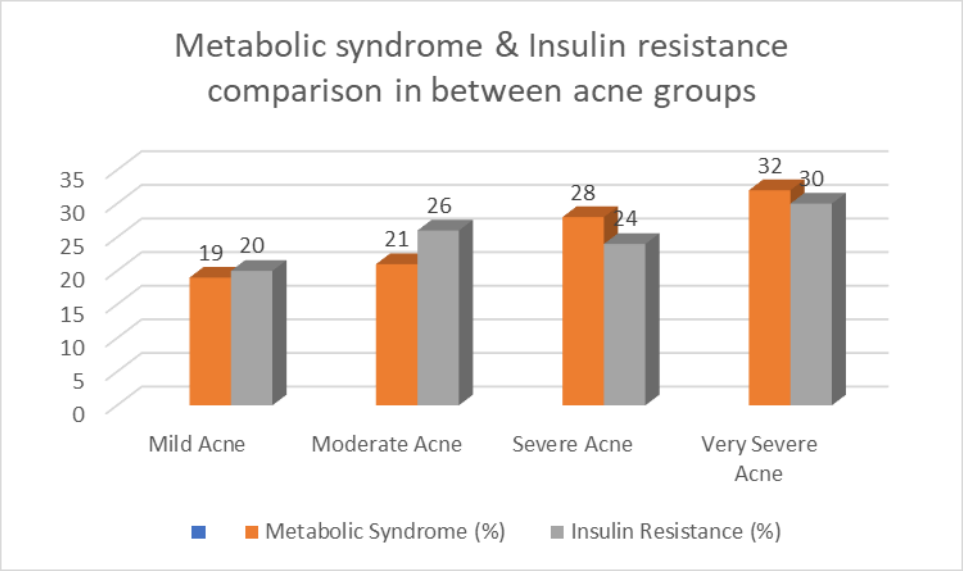

Fig.18: Metabolic syndrome & insulin resistance comparison among different acne severity group participants.

DISCUSSION

The goal of this thesis was to look into the possibility of a link between acne and insulin resistance in a group of male patients with treatment-resistant acne who were otherwise in excellent health. We opted to omit individuals who presented with metabolic syndrome based on the inclusion criteria outlined above. At least three of the following criteria must be met in order to make the diagnosis of Metabolic Syndrome: - serum triglycerides >150 mg/dl, cholesterol levels HDL 40 mg/dl (in men) or lipid-lowering medication, blood pressure greater than 130/85 mmHg or antihypertensive treatment, the presence of abdominal obesity, defined as a waistline greater than 40 inches in males; and -fasting glucose levels more than 100 mg/dl or a prior diagnosis of Diabetes Mellitus Type 2.

Insulin resistance is a well-known pathogenetic component in female patients presenting with acne and PCOS, while males have received less attention thus far. The androgenic profile was found to be normal in all males with acne evaluated here, implying that acne in these patients can be related to changes in insulin and IGF-1 circulating levels rather than changes in androgen levels, in contrast to female subjects with acne and PCOS who have hyperandrogenism and hyperinsulinemia. Despite a few research limitations, our findings support the concept that insulin resistance may play an essential role in the development of acne in males who do not respond to standard therapy. Our findings corroborate the findings of Del Prete et al. [34] and suggest that young acneic boys should be tested for insulin sensitivity before beginning dietary and/or pharmacological treatment options.

According to the current study, young male acne sufferers are more likely to have high systolic blood pressure and a higher risk of acquiring pre-diabetes. In this study, their weight and waist circumference were also shown to be greater when compared to the control group. Serum glucose and lipid levels were also shown to be higher in fasting patients (cases) as compared to the general population (controls). When the different acne severity groups were compared, the weight and systolic blood pressure were shown to increase as the severity of the acne worsened. Overall, the number of patients developing metabolic syndrome and insulin resistance in the acne group was considerably higher than in the control group.

When we compared our findings to those of Nagpal M. et al. [30], we found similarities in several of the characteristics investigated. They discovered that individuals with acne had

higher systolic and diastolic blood pressures, which is comparable to what we discovered in our current study. They also determined that adolescent acne sufferers were more likely to acquire hypertension, diabetes, and other metabolic disorders in the future.

Cerman et al. [62] discovered that a higher glycemic index was linked to acne vulgaris. The research of Emirolu N et al. 8 and Del Prete M. et al. [34] revealed that insulin resistance had a role in the pathological sequelae of acne.

Kartal D. et al. [63] conducted a research on women and discovered that using metformin, a euglycemic medicine for diabetes mellitus, by acne sufferers improved their acne symptoms. This strongly suggests a link between insulin resistance and acne.

In their study, Kumari R. et al. [24] discovered that the usage of hyperglycemic diets, which resulted in the stimulation of insulin and IGF-1-mediated P13 kinase Akt activation, produced sebaceous lipogenesis and an increase in sebocyte and keratinocytes, which might lead to acne.

According to BenAmitai D. [64], a lack of insulin-like growth factor-1 may protect against acne.

According to Alan S. [65], increasing circulating levels of androgens and a high body mass index (BMI) exacerbated the prevalence and severity of acne in female patients.

Sabat R. et al. [66] reported that there was a significant prevalence of metabolic disorders among acne patients.

According to Saleh BO. [67], elements that might boost testosterone levels, such as increased serum insulin levels such growth factor 1 and growth hormone, also increased the occurrence of acne. These people may develop hyperlipidaemia as a result of hyperandrogenism.

Although mean weight was substantially greater in individuals with severe acne compared to those with mild acne, waist circumference and body weight were not statistically different between cases and controls. Another major finding was that cases had substantially higher SBP and DBP, as well as mean fasting plasma glucose levels and serum lipids. Although the mean fasting plasma insulin level was greater in some individuals, this difference was not statistically significant. Because HOMA-IR is determined by the product of these two measures (fasting plasma glucose and insulin levels), the mean HOMA-IR value was predicted to be much higher in instances. The HOMA-IR score, on the other hand, was

comparable among acne severity groups. A significantly increased incidence of insulin resistance, defined as a HOMA-IR value more than 2.5, was seen in instances, as well as in more severe acne compared to milder acne. Furthermore, according to modified NCEP-ATP III criteria, the proportion of patients with metabolic syndrome was greater in cases than in controls, comparable to the severe acne group vs the milder acne group, and the difference was statistically significant. These final two observations of our investigation contrasted with Nagpal's work [30]. Our study's key findings may be compared to those of Nagpal's et al [30], Del Prete et al [34], and Balta et al [68].

Del Prete et al [34] recruited only 22 male patients between the ages of 15 and 26 years, with a mean age of 18.6 years. Balta et al [68] enrolled 35 male and female acne patients aged 25 and above to assess insulin resistance. The patients' average age was 30.8 years. Balta et al [68] found no statistically significant difference between patients and controls in the mean of any of the research parameters (ie, BMI, HDL-C, triglycerides, fasting plasma glucose, and insulin levels, and HOMA-IR). Del Prete et al [34] found a statistically significant difference between patients and controls in the measures SBP, DBP, fasting plasma glucose, and HOMA-IR. Furthermore, they found that cases had substantially higher BMI, waist circumference, HDL-C level, and plasma insulin level. Tsai et al. discovered a higher BMI in acne patients. [69] Alan et al [65] discovered a favourable relationship between BMI and acne severity, which is consistent with our findings. However, Balta et al [68] discovered no link between BMI and acne severity. According to modified NCEP-ATP III criteria, acne patients exhibited a greater prevalence of metabolic syndrome in our research. The prevalence of metabolic syndrome was greater in the group with extremely severe acne than in the groups with mild or moderate acne. To the best of our knowledge, no previous study has assessed the differential prevalence of metabolic syndrome depending on acne severity in a large sample size like ours.

The frequency of metabolic syndrome is strongly age related, with a rapid increase beyond the age of 60. [70] An Indian research conducted in a broad urban population in eastern part of India by Prasad et al. [71] discovered a prevalence rate of peaking at 65.6% in the age group of 60 through 69 years and 6.7% in the age group of 20 through 29 years. In our study, the prevalence of metabolic syndrome in acne patients (28.5%) was more than double that of the same age group (10.5%) in the control group. Similarly, the prevalence of extremely severe and severe acne is up to 32% and 28%, respectively. Del Prete et al [34] observed a substantially higher prevalence of metabolic syndrome in acne patients, at 36%, which was

much higher than our reported prevalence. The explanation for their study's considerably elevated frequency of metabolic syndrome might be that a diagnosis of metabolic syndrome was established even when only two of the five characteristics criteria were present instead of the required three. Another limitation of their study is the small sample size, which is deemed insufficient for determining prevalence.

In our study, the prevalence of insulin resistance in patients was reported to be 26.32%, compared to 12.3% in controls. This prevalence was raised to 30% and 24% in the very severe acne and severe acne groups, respectively, in subgroup analysis. Insulin resistance is characterised by increased insulin release as a result of diminished sensitivity. This may result in increased IGF-1, and 2 production. Acne is caused by an increase in insulin and IGF-1 levels, which are interrelated and controlled. [72]

The cross-sectional research design is one of our study's limitations. Future research targeting long term follow up of acne patients will examine the development of clinical disorders related with insulin resistance (e.g., acanthosis nigricans) and metabolic syndrome in acne patients.

CONCLUSION

When compared to controls, post-adolescent male acne patients have higher mean fasting plasma glucose levels, a greater incidence of insulin resistance, higher mean HOMA-IR values, and higher mean SBP and DBP. Body weight and blood pressure (both systolic and diastolic) are greater in people with severe grade acne. The prevalence of insulin resistance and metabolic syndrome was also shown to be substantially related to acne severity. According to our findings, post-pubertal males with acne are more likely than the general population to develop insulin resistance and metabolic disorders. Insulin resistance at a young age may be a risk factor for prediabetes and diabetes mellitus, with individuals developing hyperinsulinemia or type 2 diabetes later in life. These individuals should be monitored to see if they develop insulin resistance-related disorders.

SUMMARY

BACKGROUND:

Acne vulgaris is a chronic inflammatory condition of the pilosebaceous units with non-inflammatory and inflammatory lesions. It normally begins in adolescence and usually ends in the mid-twenties. Metabolic syndrome is a collection of changes that raises the chance of developing type 2 diabetes, arterial hypertension, and cardiovascular disease. Among the ethiopathogenic factors, peripheral insulin resistance is thought to be a causal or exacerbating factor for acne. The primary purpose of this study is to look at a possible link between acne and metabolic changes that may indicate the existence or risk of metabolic syndrome (MS).

OBJECTIVES

3. To study the clinical profile and severity of acne
4. To assess the association of metabolic syndrome and insulin resistance with acne in post adolescent male patients

MATERIALS AND METHODS

STUDY DESIGN: cross sectional study

PLACE OF STUDY: Department of Dermatology, Santosh Medical College and Hospital, Ghaziabad

STUDY POPULATION: Patients with acne vulgaris attending the outpatients' clinic of Department of Dermatology, Santosh Medical College and Hospital, Ghaziabad will be included in the study after their consent.

DURATION OF STUDY: One year

SAMPLE SIZE: 216

INCLUSION CRITERIA

1.Male Patients with acne vulgaris of age ≥20 yrs.

EXCLUSION CRITERIA

1. Patients with history of smoking and alcoholism .

2. Patients with history of Cushings syndrome

3. Patients with history of Acromegaly.

4. Oral isotretinoin therapy within past 1 year.

Detailed demographic data of all patients will be recorded in a preset proforma. History regarding onset and duration of acne, severity, aggravating factors, medical history, family history and treatment received will be taken. Written informed consent will be obtained from all the participants in the study.

RESULTS:

A total of 216 male patients were involved in the study. 108 patients with acne were selected and equal number of age matched controls were selected in this study for comparison of data.

The mean age, weight, height and waist circumference of the cases were 21.52±1.63 years, 67.14±6.27 Kg, 160.81±4.18 cm and 88.14±5.16 cm; and of controls were 22.24±2.15years, 63.40±5.21Kg, 161.27±3.71cm, and 85.49±5.36cm, respectively (p-value 0.24, <0.001, 0.8 and <0.001, respectively).

The mean systolic and diastolic blood pressures of the cases were 128.65±8.13mmHg and 82.01±7.27 mmHg, and were significantly high when compared with controls i.e. 121.57±8.29 mmHg and 74.49±6.39 mmHg, respectively (p<0.001 for both).

The mean fasting blood glucose level and HOMA-IR score of the cases were 88.33±5.44 mg/dl and 2.24±1.04, and were significantly higher than they were of controls i.e. 81.34±7.03 mg/dl and 1.84±0.63, respectively (p <0.001 and 0.003, respectively).

The mean serum triglyceride level of the cases (108.00±40.39mg/dl) was significantly higher (p=0.019) than that of controls (98.14±34.08mg/dl).

Both the groups were comparable in terms of serum HDL cholesterol levels and fasting plasma insulin concentrations (46.37±8.52mg/dl and 9.56±4.83 µIU/ml in the cases; and 44.86±8.17mg/dl and 8.33±3.07 µIU/ml in controls, p-value 0.097 and 0.059, respectively.

The percentage of metabolic syndrome was 28.48% in the cases and 10.56% of the controls and the difference was statistically significant (p=<0.001). Insulin resistance, defined as HOMA-IR score of more than 2.5, was noticed in 26.35% of the cases and 12.30% of the controls and the difference was also statistically significant (p=0.008).

The differences of mean age and weight were significantly different in four different groups of acne severity, in mild or moderate acne being the lowest and in very severe acne being the highest (p-value .05 and <.001, respectively).

The difference of systolic and diastolic blood pressure was statistically different in four acne severity groups (p-value .03 and .02, respectively), with systolic blood pressure and diastolic blood pressure being the lowest in mild acne group.

The percentage of metabolic syndrome and insulin resistance was 19% and 20% in mild acne; 21% and 26% in moderate acne; 28% and 24% in severe acne; and 32% and 30% in very severe acne groups, respectively. The differences were statistically significant (p-value .02 and .01 for metabolic syndrome and Insulin resistance, respectively).

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Annexure 1

Department of Dermatology, Venereology and Leprology,

Santosh Medical College And Hospital

CASE PERFORMA

Case no.:

Name: Age/Sex:

Marital status: Religion: Hindu/ Muslim/ Sikh/ Christian:

Address

Educational qualification: Occupation:

HISTORY:

Age of onset of acne :

Active acne: Y/N Duration: Sites:

Post acne scarring: Y/N Duration: Sites:

Precipitating / aggravating factors: Stress/ Smoking/ Diet/ Others

Treatment taken:

EXAMINATION:

GPE: Pall / Ict / Hirsutism / Cushingoid facies / Striae / Obesity

Height - Weight-

Blood Pressure- Waist circumference:

Dermatological examination:

Acne Lesions:

LOCATION	TYPE OF LESIONS	NO. OF LESIONS	FACTOR	GRADE (0-4)	LOCAL SCORE (FACTOR X GRADE)
I-FOREHEAD			2		
II-RIGHT CHEEK			2		
III-LEFT CHEEK			2		

IV-NOSE			**1**		
V-CHIN			**1**		
VI-CHEST AND UPPER BACK			**3**		

GLOBAL SCORE =

Severity= 0=None , 1-18=Mild, 19-30=Moderate, 31-38=Severe,>39 Very severe

Other cutaneous findings:

INVESTIGATIONS

1. Fasting blood sugar level-

2. Fasting Insulin level-

3. Fasting lipid profile :

i.TGL : ii. CHOLESTEROL :

iii. LDL : iv. HDL :

v. VLDL:

Metabolic Syndrome-
The metabolic syndrome defined by NCEP ATP-III[23] guidelines consists of three or more of the following:
1. Fasting plasma glucose ≥100 mg/dl (Modified for Asian men) ,

2. Serum triglycerides ≥150 mg/dl or drug treatment for elevated levels,

3. Serum HDL cholesterol <40 mg/dl or drug treatment for elevated levels ,

4. BP ≥130/85 mmHg or on BP medication or drug treatment for hypertension,

5. Waist circumference>90cm (modified for Asian men)

Insulin Resistance- Fasting Insulin (Microunits per Milliliter) × Fasting Glucose (Micograms per Deciliter)/405.A HOMA-IR value greater than 2.5 is predefined arbitrarily as insulin resistance.

ANNEXURE 2

FORM OF INFORMED CONSENT

Name of the patient: Age:

Address: Phone Number:

S.NO: Date:

I have been explained the details of the study entitled **"Study Of Clinical Profile Of Acne In Post- Adolescent Males and its Association With Metabolic Syndrome And Insulin Resistance"** and my questions regarding the study have been answered to my satisfaction in a language understood by me.

1. I understand that I have the right to withdraw from the study at anytime and to decline to answer any particular question.
2. I understand that my participation in this study is confidential and that no material that could identify me will be used in the analysis and in any reports based on this study.

I hereby provide my consent in the study entitled **"Study Of Clinical Profile Of Acne In Post- Adolescent Males and its Association With Metabolic Syndrome And Insulin Resistance"**

Signature of patient

Name: Date:

We have witnessed that the patient signed the above form in the presence of his free will after fully having understood its contents.

Signature of witness Signature of Investigator

Name Name

Relation Designation

ANNEXURE 3:

The metabolic syndrome defined by NCEP ATP-III guidelines consists of three or more of the following:

1. Fasting plasma glucose ≥100 mg/dl (Modified for Asian men) ,

2. Serum triglycerides ≥150 mg/dl or drug treatment for elevated levels,

3. Serum HDL cholesterol <40 mg/dl or drug treatment for elevated levels ,

4. BP ≥130/85 mmHg or on BP medication or drug treatment for hypertension,

5. Waist circumference>90cm (modified for Asian men).

ANNEXURE 4:

Assessment of acne will be done using a method **Global Acne Grading System:** 6 locations are selected on face / chest / upper back. Each location is graded on 0-4

LOCATION		FACTOR
I.	Forehead.	2
II.	Right cheek.	2
III.	Left cheek.	2
IV.	Nose	1
V.	Chin.	1
VI.	Chest and upper back	3

Each location is graded on 0-4; with the most severe lesion determining grade for that area:

(0 No lesions; 1 ≥one comedonc ; 2.≥one papule; 3≥one pustule; 4 .≥one nodule)

Grade X Factor = local score

Global Score = sum of all the local scores.

Global score:

0=None

1-18=Mild

19-30=Moderate

31-38=Severe

>39 Very severe

ANNEXURE 5:

The HOMA-IR (Homeostasis Model Assessment–Insulin Resistance) values will be calculated using the following formula:

Fasting Insulin (Microunits per Milliliter) × Fasting Glucose (Micograms per Deciliter)/405.

A HOMA-IR value greater than 2.5 is predefined arbitrarily as insulin resistance.

Ouriginal
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Document Information

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SANTOSH
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(Established u/s 3 of the UGC Act, 1956)

F. No. SU/2022/1751[10]

Dated: 05.08.2022

Subject: Grant of Ethical Clearance for Thesis Protocol Topic "**Study Of Clinical Profile Of Acne In Post-Adolescent Males and Its Association With Metabolic Syndrome And Insulin Resistance**", submitted by **Dr. Garima Yadav,** MD/MS student of Batch 2020-2021, Department of **Dermatology**.

*****

With reference to his/her request for grant of Ethical Clearance for the Thesis Protocol entitled "**Study Of Clinical Profile Of Acne In Post-Adolescent Males and Its Association With Metabolic Syndrome And Insulin Resistance**", **Dr. Garima Yadav** is informed that the Thesis Protocol submitted by him/her was considered by the **Screening Committee** of the Santosh Medical College & Hospital. The recommendations of the **Screening Committee** were considered in detail by the Institutional **Ethics Committee** in its meeting held on **22.07.2022** and the same was **approved** by the **Ethics Committee.**

He /She is informed accordingly for further necessary action.

[DR. ALPANA AGRAWAL]
REGISTRAR

SANTOSH DEEMED TO BE UNIVERSITY REGISTRAR GHAZIABAD, NCR DELHI

Dr. Garima Yadav,
MD/MS student of batch 2020-2021
Department of Dermatology
Email: garima.seeker@yahoo.com

Copy to:

1. The Vice Chancellor
2. The Dean, SMC&H
3. The Dean – Research
4. The Dean – Academics
5. The Director - IQAC
6. Dr. V.K.Garg (Guide)
7. HOD of **Dermatology**

MASTER CHART

ubj no	Age	Sex	Marital st	Religion	Occupati	Age of on	Active	acation	mot	Sites	che scarr	ion	me	Sites	ld Pressur	ld Pressur	circumfer	eight (cm	Weight	rept. facto	atment fat	LOBAL st.	bld sugt	Insulin l	TG Level	HDL leve	MA-IR	vthotic syndrome	
1	20	M	UM	HINDU	student	20	Y	1	nin, forehea		Y	1	nin, forehea		120	78	80	168	70	STRESS	NIL	10	86	9.8	109	40	2.9	N	
2	20	M	UM	HINDU	student	20	Y	0.5	ft cheek, n		Y	0.5	ft cheek, n		130	84	92	166	85	SMOKING	NIL	40	120	11.4	118	34	2.7	Y	
3	20	M	UM	HINDU	student	20	Y	2	, back, nose		Y	2	, back, nose		124	80	78	170	72	SMOKING	RNESS CRE	14	78	9.4	112	49	2.8	Y	
4	21	M	UM	HINDU	student	21	N	4	ft cheek, n		N	4	ft cheek, n		110	68	82	174	65	SMOKING	NIL	18	88	8.9	102	40	2.7	N	
5	22	M	UM	HINDU	student	22	N	5	k, nose, for		N	5	k, nose, for		118	70	86	168	67	STRESS	NIL	10	90	9	104	48	2.4	N	
6	21	M	UM	HINDU	student	21	N	2	, back, nose		N	2	, back, nose		126	84	90	165	90	STRESS	ULTIVITAM	38	92	9.6	110	42	2.2	N	
7	20	M	UM	HINDU	student	20	Y	3	, chin, nose		Y	3	, chin, nose		122	78	84	176	82	DIET	NIL	25	78	9.8	113	46	2.7	N	
8	22	M	M	HINDU	student	22	Y	3	ead, nose,		Y	3	ead, nose,		126	80	88	166	72	DIET	RNESS CRE	16	80	10	109	40	2.2	N	
9	20	M	UM	HINDU	student	20	Y	1	, chin, nose		Y	1	, chin, nose		110	70	80	169	68	DIET	ULTIVITAM	24	89	9.6	107	46	2.1	N	
10	20	M	UM	HINDU	student	20	Y	4	. forehead,		Y	4	. forehead,		134	88	94	167	92	SMOKING	RNESS CRE	42	99	10.1	113	41	2.8	N	
11	21	M	UM	HINDU	student	21	Y	6	nin, forehea		Y	6	nin, forehea		140	90	96	165	90	STRESS	ULTIVITAM	40	100	10.7	116	42	2.6	Y	
12	21	M	UM	HINDU	student	21	Y	7	ft cheek, n		Y	7	ft cheek, n		134	88	92	165	88	SMOKING	NIL	41	92	9.1	108	49	2.4	N	
13	23	M	M	HINDU	profession	19	N	5	, back, nose		N	5	, back, nose		128	84	91	168	89	SMOKING	NIL	44	90	8.9	106	44	2.6	N	
14	24	M	M	HINDU	profession	20	N	2	ft cheek, n		N	2	ft cheek, n		126	86	90	169	85	DIET	NIL	40	92	9.2	103	45	2.1	N	
15	22	M	UM	HINDU	student	22	Y	8	k, nose, for		Y	8	k, nose, for		114	70	80	170	76	STRESS	ULTIVITAM	38	94	9.5	104	42	2.2	Y	
16	21	M	UM	HINDU	student	21	Y	6	, back, nose		Y	6	, back, nose		120	70	84	174	71	STRESS	RNESS CRE	34	88	9.9	111	40	2.3	Y	
17	22	M	UM	HINDU	student	22	Y	9	, chin, nose		Y	9	, chin, nose		116	68	80	173	67	SMOKING	RNESS CRE	30	90	9.4	110	34	2.3	N	
18	23	M	M	HINDU	profession	23	Y	12	ead, nose,		Y	12	ead, nose,		118	76	80	172	65	SMOKING	ULTIVITAM	18	79	8.8	103	49	2.1	N	
19	20	M	UM	HINDU	profession	20	Y	4	, chin, nose		Y	4	, chin, nose		124	80	82	175	69	STRESS	NIL	26	85	9.6	110	40	2.1	N	
20	20	M	UM	HINDU	student	20	Y	4	. forehead,		Y	4	. forehead,		128	88	90	168	90	OTHER	NIL	31	83	9.4	109	48	2.9	Y	
21	20	M	UM	HINDU	student	20	Y	6	nin, forehea		Y	6	nin, forehea		130	78	91	166	92	STRESS	ULTIVITAM	34	90	9	118	42	2.7	N	
22	20	M	UM	HINDU	student	20	Y	6	ft cheek, n		Y	6	ft cheek, n		134	84	94	166	93	SMOKING	RNESS CRE	35	92	9.2	112	46	2.8	Y	
23	21	M	UM	HINDU	student	21	Y	8	, back, nose		Y	8	, back, nose		136	90	93	164	90	SMOKING	ULTIVITAM	40	86	11.2	102	40	2.7	Y	
24	22	M	UM	HINDU	student	22	Y	10	ft cheek, n		Y	10	ft cheek, n		106	60	80	170	68	SMOKING	NIL	14	85	9.6	104	46	2.4	N	
25	22	M	UM	HINDU	student	22	N	16	k, nose, for		N	16	k, nose, for		114	60	78	170	65	STRESS	NIL	18	90	9.6	110	41	2.2	N	
26	24	M	M	MUSLIM	profession	24	N	24	, back, nose		N	24	, back, nose		120	80	81	174	70	DIET	NIL	22	95	9.8	113	42	2.7	N	
27	20	M	UM	MUSLIM	profession	20	Y	3	, chin, nose		Y	3	, chin, nose		122	82	83	171	65	DIET	RNESS CRE	24	92	9.5	109	49	2.2	N	
28	20	M	UM	HINDU	profession	20	N	5	ead, nose,		N	5	ead, nose,		130	84	90	168	89	SMOKING	RNESS CRE	40	98	9.8	107	44	2.1	N	
29	21	M	UM	MUSLIM	profession	21	Y	9	, chin, nose		Y	9	, chin, nose		128	86	91	165	90	STRESS	ULTIVITAM	43	108	9.4	113	45	2.8	N	
30	20	M	UM	MUSLIM	student	20	Y	5	. forehead,		Y	5	. forehead,		120	78	80	168	70	STRESS	NIL	10	86	9.8	116	42	2.6	N	
31	20	M	UM	HINDU	student	20	Y	5	nin, forehea		Y	5	nin, forehea		130	84	92	166	85	SMOKING	NIL	12	120	11.4	108	40	2.4	Y	
32	20	M	UM	HINDU	student	20	N	3	ft cheek, n		N	3	ft cheek, n		124	80	78	170	72	SMOKING	RNESS CRE	14	78	9.4	106	34	2.6	N	
33	21	M	UM	HINDU	student	21	Y	7	, back, nose		Y	7	, back, nose		110	68	82	174	65	SMOKING	NIL	18	88	8.9	103	49	2.1	N	
34	21	M	UM	HINDU	student	21	Y	6	ft cheek, n		Y	6	ft cheek, n		118	70	86	168	67	STRESS	NIL	10	90	9	104	40	2.2	N	
35	21	M	UM	MUSLIM	student	21	Y	5	k, nose, for		Y	5	k, nose, for		126	84	90	165	90	STRESS	ULTIVITAM	38	92	9.6	111	48	2.3	Y	
36	23	M	UM	MUSLIM	profession	23	Y	11	, back, nose		Y	11	, back, nose		122	78	84	176	82	DIET	NIL	25	78	9.8	110	42	2.3	Y	
37	24	M	M	MUSLIM	profession	24	N	18	, chin, nose		N	18	, chin, nose		126	80	88	166	72	DIET	RNESS CRE	16	80	10	103	46	2.1	N	
38	22	M	UM	HINDU	profession	22	Y	12	ead, nose,		Y	12	ead, nose,		110	70	80	169	68	DIET	ULTIVITAM	24	89	9.6	110	40	2.1	N	
39	21	M	UM	HINDU	profession	21	Y	10	, chin, nose		Y	10	, chin, nose		134	88	94	167	92	SMOKING	RNESS CRE	42	99	10.1	109	46	2.9	N	
40	20	M	UM	CHRISCHIA	profession	20	Y	6	. forehead,		Y	6	. forehead,		140	90	96	165	90	STRESS	ULTIVITAM	40	100	10.7	118	41	2.7	Y	
41	20	M	UM	HINDU	profession	20	Y	6	nin, forehea		Y	6	nin, forehea		134	88	92	165	88	SMOKING	NIL	41	92	9.1	112	42	2.8	N	
42	20	M	UM	HINDU	student	20	Y	6	ft cheek, n		Y	6	ft cheek, n		128	84	91	168	89	SMOKING	NIL	44	90	8.9	102	49	2.7	Y	
43	20	M	UM	HINDU	student	20	Y	4	, back, nose		Y	4	, back, nose		126	86	90	169	85	DIET	NIL	40	92	9.2	104	44	2.4	Y	
44	20	M	UM	HINDU	student	20	Y	3	ft cheek, n		Y	3	ft cheek, n		114	70	80	170	76	STRESS	ULTIVITAM	38	94	9.5	110	45	2.2	N	
45	20	M	UM	MUSLIM	student	20	Y	2	k, nose, for		Y	2	k, nose, for		120	70	84	174	71	STRESS	RNESS CRE	34	88	9.9	113	42	2.7	N	
46	21	M	UM	HINDU	student	21	Y	1	, back, nose		Y	1	, back, nose		116	68	80	173	67	SMOKING	RNESS CRE	30	90	9.4	109	40	2.2	N	
47	22	M	UM	HINDU	student	22	Y	8	, chin, nose		Y	8	, chin, nose		118	76	80	172	65	SMOKING	ULTIVITAM	18	79	8.8	107	34	2.1	N	
48	23	M	UM	HINDU	profession	23	N	10	ead, nose,		N	10	ead, nose,		124	80	82	175	69	STRESS	NIL	26	85	9.6	113	49	2.8	N	
49	22	M	UM	CHRISCHIA	profession	22	Y	12	, chin, nose		Y	12	, chin, nose		128	88	90	168	90	OTHER	NIL	31	83	9.4	116	40	2.6	N	
50	22	M	UM	MUSLIM	profession	22	Y	16	. forehead,		Y	16	. forehead,		130	78	91	166	92	STRESS	ULTIVITAM	34	90	9	108	48	2.4	N	
51	22	M	UM	HINDU	profession	22	Y	16	nin, forehea		Y	16	nin, forehea		134	84	94	166	93	SMOKING	RNESS CRE	35	92	9.2	106	42	2.6	Y	
52	21	M	UM	HINDU	profession	21	Y	14	ft cheek, n		Y	14	ft cheek, n		136	90	93	164	90	SMOKING	ULTIVITAM	40	86	11.2	103	46	2.1	N	
53	20	M	UM	HINDU	student	20	Y	6	, back, nose		Y	6	, back, nose		106	60	80	170	68	SMOKING	NIL	14	85	9.6	104	40	2.2	N	
54	20	M	UM	MUSLIM	student	20	Y	4	ft cheek, n		Y	4	ft cheek, n		114	60	78	170	65	STRESS	NIL	18	90	9.6	111	46	2.3	N	
55	21	M	UM	MUSLIM	student	21	Y	6	k, nose, for		Y	6	k, nose, for		120	80	81	174	70	DIET	NIL	22	95	9.8	110	41	2.3	Y	
56	20	M	UM	HINDU	student	20	Y	7	, back, nose		Y	7	, back, nose		122	82	83	171	65	DIET	RNESS CRE	24	92	9.5	103	42	2.1	Y	
57	22	M	UM	HINDU	student	22	N	14	, chin, nose		N	14	, chin, nose		130	84	90	168	89	SMOKING	RNESS CRE	40	98	9.8	110	49	2.1	N	
58	23	M	UM	HINDU	profession	23	N	18	ead, nose,		N	18	ead, nose,		128	86	91	165	90	STRESS	ULTIVITAM	43	108	9.4	109	44	2.9	N	
59	24	M	UM	HINDU	profession	24	N	20	, chin, nose		N	20	, chin, nose		120	78	80	168	70	STRESS	NIL	10	86	9.8	118	45	2.7	N	
60	21	M	UM	MUSLIM	profession	21	Y	2	. forehead,		Y	2	. forehead,		130	84	92	166	85	SMOKING	NIL	12	120	11.4	112	42	2.8	Y	
61	22	M	UM	MUSLIM	profession	22	N	12	nin, forehea		N	12	nin, forehea		124	80	78	170	72	SMOKING	RNESS CRE	14	78	9.4	102	40	2.7	N	
62	22	M	UM	HINDU	student	22	N	13	ft cheek, n		N	13	ft cheek, n		110	68	82	174	65	SMOKING	NIL	18	88	8.9	104	34	2.4	Y	
63	21	M	UM	HINDU	student	21	Y	10	, back, nose		Y	10	, back, nose		118	70	86	168	67	STRESS	NIL	10	90	9	110	49	2.2	Y	
64	21	M	UM	HINDU	student	21	Y	9	ft cheek, n		Y	9	ft cheek, n		126	84	90	165	90	STRESS	ULTIVITAM	38	92	9.6	113	40	2.7	N	
65	20	M	UM	HINDU	student	20	Y	6	k, nose, for		Y	6	k, nose, for		122	78	84	176	82	DIET	NIL	25	78	9.8	109	48	2.2	N	
66	20	M	UM	CHRISCHIA	student	20	Y	6	, back, nose		Y	6	, back, nose		126	80	88	166	72	DIET	RNESS CRE	16	80	10	107	42	2.1	N	
67	21	M	UM	HINDU	student	21	Y	4	, chin, nose		Y	4	, chin, nose		110	70	80	169	68	DIET	ULTIVITAM	24	89	9.6	113	46	2.8	N	
68	21	M	UM	HINDU	student	21	Y	8	ead, nose,		Y	8	ead, nose,		134	88	94	167	92	SMOKING	RNESS CRE	42	99	10.1	116	40	2.6	N	
69	20	M	UM	HINDU	student	20	Y	7	, chin, nose		Y	7	, chin, nose		140	90	96	165	90	STRESS	ULTIVITAM	40	100	10.7	108	46	2.4	N	
70	23	M	UM	MUSLIM	student	23	Y	12	. forehead,		Y	12	. forehead,		134	88	92	165	88	SMOKING	NIL	41	92	9.1	106	41	2.6	N	
71	23	M	UM	HINDU	profession	23	N	16	nin, forehea		N	16	nin, forehea		128	84	91	168	89	SMOKING	NIL	44	90	8.9	103	42	2.1	Y	
72	21	M	UM	HINDU	student	21	N	10	ft cheek, n		N	10	ft cheek, n		126	86	90	169	85	DIET	NIL	40	92	9.2	104	49	2.2	N	
73	21	M	UM	HINDU	student	21	N	11	, back, nose		N	11	, back, nose		114	70	80	170	76	STRESS	ULTIVITAM	38	94	9.5	111	44	2.3	N	
74	20	M	UM	CHRISCHIA	student	20	Y	8	ft cheek, n		Y	8	ft cheek, n		120	70	84	174	71	STRESS	RNESS CRE	34	88	9.9	110	45	2.3	N	

75	20 M	UM	CHRISCHIA	student	20 Y	10	', nose, for	Y	10	', nose, for	116	68	80	173	67	SMOKING	RNESS CRE	30	90	9.4	103	42	2.1	Y
76	21 M	UM	MUSLIM	student	21 Y	11	, back, nose	Y	11	, back, nose	118	76	80	172	65	SMOKING	ULTIVITAM	18	79	8.8	110	40	2.1	Y
77	21 M	UM	HINDU	student	21 Y	12	., chin, nose	Y	12	., chin, nose	124	80	82	175	69	STRESS	NIL	26	85	9.6	109	34	2.9	N
78	22 M	UM	HINDU	student	22 Y	13	ead, nose,	Y	13	ead, nose,	128	88	90	168	90	OTHER	NIL	31	83	9.4	118	49	2.7	N
79	21 M	UM	MUSLIM	student	21 Y	9	., chin, nose	Y	9	., chin, nose	130	78	91	166	92	STRESS	ULTIVITAM	34	90	9	112	40	2.8	N
80	21 M	UM	HINDU	student	21 Y	10	forehead,	Y	10	forehead,	134	84	94	166	93	SMOKING	RNESS CRE	35	92	9.2	102	48	2.7	Y
81	21 M	UM	HINDU	student	21 Y	8	in, forehe	Y	8	in, forehe	136	90	93	164	90	SMOKING	ULTIVITAM	40	86	11.2	104	42	2.4	N
82	22 M	UM	HINDU	student	22 Y	9	lt cheek, n	Y	9	lt cheek, n	106	60	80	170	68	SMOKING	NIL	14	85	9.6	110	46	2.2	Y
83	23 M	UM	HINDU	student	23 N	18	, back, nose	N	18	, back, nose	114	60	78	170	65	STRESS	NIL	18	90	9.6	113	40	2.7	Y
84	22 M	UM	HINDU	student	22 N	13	lt cheek, n	N	13	lt cheek, n	120	80	81	174	70	DIET	NIL	22	95	9.8	109	46	2.2	N
85	21 M	UM	MUSLIM	profession	21 Y	10	', nose, for	Y	10	', nose, for	122	82	83	171	65	DIET	RNESS CRE	24	92	9.5	107	41	2.1	N
86	20 M	UM	HINDU	profession	20 Y	10	, back, nose	Y	10	, back, nose	130	84	90	168	89	SMOKING	RNESS CRE	40	98	9.8	113	42	2.8	N
87	20 M	UM	HINDU	student	20 Y	4	., chin, nose	Y	4	., chin, nose	128	86	91	165	90	STRESS	ULTIVITAM	43	108	9.4	116	49	2.6	N
88	20 M	UM	HINDU	student	20 Y	6	ead, nose,	Y	6	ead, nose,	120	78	80	168	70	STRESS	NIL	10	86	9.8	108	44	2.4	N
89	21 M	UM	HINDU	student	21 Y	8	., chin, nose	Y	8	., chin, nose	130	84	92	166	85	SMOKING	NIL	12	120	11.4	106	45	2.6	N
90	22 M	UM	HINDU	profession	22 Y	9	forehead,	Y	9	forehead,	124	80	78	170	72	SMOKING	RNESS CRE	14	78	9.4	103	42	2.1	N
91	22 M	UM	CHRISCHIA	profession	22 N	10	in, forehe	N	10	in, forehe	110	68	82	174	65	SMOKING	NIL	18	88	8.9	104	40	2.2	Y
92	23 M	UM	HINDU	profession	23 N	14	lt cheek, n	N	14	lt cheek, n	118	70	86	168	67	STRESS	NIL	10	90	9	111	34	2.3	N
93	24 M	UM	HINDU	profession	20 N	4	, back, nose	N	4	, back, nose	126	84	90	165	90	STRESS	ULTIVITAM	38	92	9.6	110	49	2.3	N
94	25 M	UM	HINDU	profession	20 N	6	lt cheek, n	N	6	lt cheek, n	122	78	84	176	82	DIET	NIL	25	78	9.8	103	40	2.1	N
95	21 M	UM	MUSLIM	profession	21 N	8	', nose, for	N	8	', nose, for	126	80	88	166	72	DIET	RNESS CRE	16	80	10	110	48	2.1	Y
96	22 M	UM	HINDU	profession	22 N	9	, back, nose	N	9	, back, nose	110	70	80	169	68	DIET	ULTIVITAM	24	89	9.6	109	42	2.9	Y
97	21 M	UM	HINDU	student	21 Y	10	., chin, nose	Y	10	., chin, nose	134	88	94	167	92	SMOKING	RNESS CRE	42	99	10.1	118	46	2.7	N
98	20 M	UM	HINDU	student	20 Y	8	ead, nose,	Y	8	ead, nose,	140	90	96	165	90	STRESS	ULTIVITAM	40	100	10.7	112	40	2.8	N
99	20 M	UM	HINDU	student	20 Y	6	., chin, nose	Y	6	., chin, nose	134	88	92	165	88	SMOKING	NIL	41	92	9.1	102	46	2.7	N
100	23 M	UM	CHRISCHIA	profession	23 Y	11	forehead,	Y	11	forehead,	128	84	91	168	89	SMOKING	NIL	44	90	8.9	104	41	2.4	Y
101	25 M	M	HINDU	profession	20 N	10	in, forehe	N	10	in, forehe	126	86	90	169	85	DIET	NIL	40	92	9.2	110	42	2.2	N
102	21 M	UM	HINDU	student	21 Y	6	lt cheek, n	Y	6	lt cheek, n	114	70	80	170	76	STRESS	ULTIVITAM	38	94	9.5	113	49	2.7	Y
103	22 M	UM	CHRISCHIA	student	22 Y	11	, back, nose	Y	11	, back, nose	120	70	84	174	71	STRESS	RNESS CRE	34	88	9.9	109	44	2.2	Y
104	20 M	UM	HINDU	student	20 Y	6	lt cheek, n	Y	6	lt cheek, n	116	68	80	173	67	SMOKING	RNESS CRE	30	90	9.4	107	45	2.1	N
105	20 M	UM	MUSLIM	student	20 Y	4	', nose, for	Y	4	', nose, for	118	76	80	172	65	SMOKING	ULTIVITAM	18	79	8.8	113	42	2.8	N
106	20 M	UM	HINDU	student	20 Y	4	, back, nose	Y	4	, back, nose	124	80	82	175	69	STRESS	NIL	26	85	9.6	116	40	2.6	N
107	20 M	UM	HINDU	student	20 Y	4	., chin, nose	Y	4	., chin, nose	128	88	90	168	90	OTHER	NIL	31	83	9.4	108	34	2.4	N
108	20 M	UM	HINDU	student	20 Y	3	ead, nose,	Y	3	ead, nose,	130	78	91	166	92	NIL	NIL	NIL	30	90	9	98	49	2	N
109	20 M	UM	MUSLIM	student	20 N	0	NA	N	0	NA	134	84	94	166	93	NIL	NIL	NIL	NA	92	9.2	96	40	2.1	N
110	20 M	UM	MUSLIM	student	20 N	0	NA	N	0	NA	136	90	93	164	90	NIL	NIL	NIL	NA	86	7.6	104	48	2.2	N
111	20 M	UM	HINDU	student	20 N	0	NA	N	0	NA	106	60	80	170	68	NIL	NIL	NIL	NA	85	8.6	96	42	2.3	N
112	20 M	UM	HINDU	student	20 N	0	NA	N	0	NA	114	60	78	170	65	NIL	NIL	NIL	NA	90	8.8	94	46	2.3	N
113	21 M	UM	HINDU	student	21 N	0	NA	N	0	NA	120	80	81	174	70	NIL	NIL	NIL	NA	95	9.1	93	40	2.1	N
114	22 M	UM	CHRISCHIA	student	22 N	0	NA	N	0	NA	122	82	83	171	65	NIL	NIL	NIL	NA	92	8.5	90	46	2.1	N
115	21 M	UM	HINDU	student	21 N	0	NA	N	0	NA	130	84	90	168	89	NIL	NIL	NIL	NA	98	8.8	93	41	1.6	Y
116	20 M	UM	HINDU	student	20 N	0	NA	N	0	NA	128	86	91	165	90	NIL	NIL	NIL	NA	80	8.4	96	42	1.4	N
117	22 M	UM	HINDU	student	22 N	0	NA	N	0	NA	120	78	80	168	70	NIL	NIL	NIL	NA	86	8.2	99	49	1.3	N
118	24 M	UM	HINDU	student	20 N	0	NA	N	0	NA	130	84	92	166	85	NIL	NIL	NIL	NA	82	8.8	101	44	1.6	N
119	21 M	UM	HINDU	student	21 N	0	NA	N	0	NA	124	80	78	170	72	NIL	NIL	NIL	NA	78	9	95	45	1.7	N
120	20 M	UM	HINDU	student	20 N	0	NA	N	0	NA	110	68	82	174	65	NIL	NIL	NIL	NA	88	9.2	96	42	1.8	Y
121	21 M	UM	HINDU	student	21 N	0	NA	N	0	NA	118	70	86	168	67	NIL	NIL	NIL	NA	90	7.6	98	40	1.8	N
122	23 M	UM	HINDU	student	19 N	0	NA	N	0	NA	126	84	90	165	90	NIL	NIL	NIL	NA	92	8.6	96	34	1.6	N
123	24 M	M	HINDU	student	20 N	0	NA	N	0	NA	122	78	84	176	82	NIL	NIL	NIL	NA	78	8.8	104	49	1.9	N
124	22 M	UM	HINDU	student	22 N	0	NA	N	0	NA	126	80	88	166	72	NIL	NIL	NIL	NA	80	9.1	96	40	2.1	N
125	21 M	UM	HINDU	student	21 N	0	NA	N	0	NA	110	70	80	169	68	NIL	NIL	NIL	NA	89	8.5	94	48	2	N
126	22 M	UM	HINDU	profession	22 N	0	NA	N	0	NA	134	88	94	167	92	NIL	NIL	NIL	NA	99	8.8	93	42	2.1	N
127	23 M	UM	HINDU	profession	23 N	0	NA	N	0	NA	140	90	96	165	90	NIL	NIL	NIL	NA	80	8.4	90	46	1.7	N
128	20 M	UM	HINDU	student	20 N	0	NA	N	0	NA	134	88	92	165	88	NIL	NIL	NIL	NA	92	8.2	93	40	1.9	Y
129	20 M	UM	HINDU	student	20 N	0	NA	N	0	NA	128	84	91	168	89	NIL	NIL	NIL	NA	90	8.8	96	46	1.8	N
130	20 M	UM	HINDU	student	20 N	0	NA	N	0	NA	126	86	90	169	85	NIL	NIL	NIL	NA	92	9	99	41	2	N
131	20 M	UM	HINDU	profession	20 N	0	NA	N	0	NA	114	70	80	170	76	NIL	NIL	NIL	NA	94	9.2	101	42	2.1	N
132	21 M	UM	HINDU	profession	21 N	0	NA	N	0	NA	120	70	84	174	71	NIL	NIL	NIL	NA	88	7.6	95	49	2.2	N
133	22 M	UM	HINDU	student	22 N	0	NA	N	0	NA	116	68	80	173	67	NIL	NIL	NIL	NA	90	8.6	96	44	2.3	Y
134	22 M	UM	HINDU	student	22 N	0	NA	N	0	NA	118	76	80	172	65	NIL	NIL	NIL	NA	79	8.8	98	45	2.3	N
135	24 M	M	HINDU	student	20 N	0	NA	N	0	NA	124	80	82	175	69	NIL	NIL	NIL	NA	85	9.1	96	42	2.1	N
136	20 M	UM	HINDU	student	20 N	0	NA	N	0	NA	128	88	90	168	90	NIL	NIL	NIL	NA	83	8.5	104	40	2.1	N
137	20 M	UM	HINDU	student	20 N	0	NA	N	0	NA	130	78	91	166	92	NIL	NIL	NIL	NA	90	8.8	96	34	1.6	N

138	21 M	UM	HINDU	student	21 N	0	NA	N	0	NA	134	84	94	166	93	NIL	NIL	NA	92	8.4	94	49	1.4	N
139	20 M	UM	HINDU	profession	21 N	0	NA	N	0	NA	136	90	93	164	90	NIL	NIL	NA	86	8.2	93	40	1.3	N
140	20 M	UM	HINDU	profession	20 N	0	NA	N	0	NA	106	60	80	170	68	NIL	NIL	NA	85	8.8	90	48	1.6	N
141	20 M	UM	HINDU	profession	20 N	0	NA	N	0	NA	114	60	78	170	65	NIL	NIL	NA	90	9	93	42	1.7	Y
142	21 M	UM	HINDU	profession	21 N	0	NA	N	0	NA	120	80	81	174	70	NIL	NIL	NA	95	9.2	96	46	1.8	N
143	21 M	UM	MUSLIM	student	21 N	0	NA	N	0	NA	122	82	83	171	65	NIL	NIL	NA	92	7.6	99	40	1.8	N
144	21 M	UM	MUSLIM	student	21 N	0	NA	N	0	NA	130	84	90	168	89	NIL	NIL	NA	98	8.6	101	46	1.6	N
145	23 M	UM	HINDU	student	23 N	0	NA	N	0	NA	128	86	91	165	90	NIL	NIL	NA	80	8.8	95	41	1.9	N
146	24 M	M	MUSLIM	student	24 N	0	NA	N	0	NA	120	78	80	168	70	NIL	NIL	NA	82	9.1	96	42	2.1	Y
147	22 M	UM	MUSLIM	student	22 N	0	NA	N	0	NA	130	84	92	166	85	NIL	NIL	NA	78	8.5	98	49	2	N
148	21 M	UM	HINDU	student	21 N	0	NA	N	0	NA	124	80	78	170	72	NIL	NIL	NA	88	8.8	96	44	2.1	N
149	20 M	UM	HINDU	profession	20 N	0	NA	N	0	NA	110	68	82	174	65	NIL	NIL	NA	90	8.4	104	45	1.7	N
150	20 M	UM	HINDU	profession	20 N	0	NA	N	0	NA	118	70	86	168	67	NIL	NIL	NA	92	8.2	96	42	1.9	N
151	20 M	UM	HINDU	profession	20 N	0	NA	N	0	NA	126	84	90	165	90	NIL	NIL	NA	78	8.8	94	40	1.8	N
152	20 M	UM	MUSLIM	profession	20 N	0	NA	N	0	NA	122	78	84	176	82	NIL	NIL	NA	80	9	93	34	2	N
153	20 M	UM	MUSLIM	profession	20 N	0	NA	N	0	NA	126	80	88	166	72	NIL	NIL	NA	89	9.2	90	49	2.1	N
154	20 M	UM	MUSLIM	profession	20 N	0	NA	N	0	NA	110	70	80	169	68	NIL	NIL	NA	99	7.6	93	40	2.2	Y
155	21 M	UM	HINDU	student	21 N	0	NA	N	0	NA	134	88	94	167	92	NIL	NIL	NA	80	8.6	96	48	2.3	N
156	22 M	UM	HINDU	student	22 N	0	NA	N	0	NA	140	90	96	165	90	NIL	NIL	NA	92	8.8	99	42	2.3	N
157	23 M	UM	CHRISCHIA	student	23 N	0	NA	N	0	NA	134	88	92	165	88	NIL	NIL	NA	90	9.1	101	46	2.1	N
158	22 M	UM	HINDU	student	22 N	0	NA	N	0	NA	128	84	91	168	89	NIL	NIL	NA	92	8.5	95	40	2.1	N
159	22 M	UM	HINDU	student	22 N	0	NA	N	0	NA	126	86	90	169	85	NIL	NIL	NA	94	8.8	96	46	1.6	Y
160	22 M	UM	HINDU	student	22 N	0	NA	N	0	NA	114	70	80	170	76	NIL	NIL	NA	88	8.4	98	41	1.4	N
161	21 M	UM	HINDU	profession	21 N	0	NA	N	0	NA	120	70	84	174	71	NIL	NIL	NA	90	8.2	96	42	1.3	N
162	20 M	UM	MUSLIM	profession	20 N	0	NA	N	0	NA	116	68	80	173	67	NIL	NIL	NA	79	8.8	104	49	1.6	N
163	20 M	UM	HINDU	profession	20 N	0	NA	N	0	NA	118	76	80	172	65	NIL	NIL	NA	85	9	96	44	1.7	N
164	21 M	UM	HINDU	profession	21 N	0	NA	N	0	NA	124	80	82	175	69	NIL	NIL	NA	83	9.2	94	45	1.8	N
165	20 M	UM	HINDU	profession	20 N	0	NA	N	0	NA	128	88	90	168	90	NIL	NIL	NA	90	7.6	93	42	1.8	N
166	22 M	UM	CHRISCHIA	student	22 N	0	NA	N	0	NA	130	78	91	166	92	NIL	NIL	NA	92	8.6	90	40	1.6	N
167	23 M	UM	MUSLIM	student	23 N	0	NA	N	0	NA	134	84	94	166	93	NIL	NIL	NA	86	8.8	93	34	1.9	Y
168	24 M	M	HINDU	student	24 N	0	NA	N	0	NA	136	90	93	164	90	NIL	NIL	NA	85	9.1	96	49	2.1	N
169	21 M	UM	HINDU	student	21 N	0	NA	N	0	NA	106	60	80	170	68	NIL	NIL	NA	90	8.5	99	40	2	N
170	22 M	UM	HINDU	student	22 N	0	NA	N	0	NA	114	60	78	170	65	NIL	NIL	NA	95	8.8	101	48	2.1	N
171	22 M	UM	MUSLIM	profession	22 N	0	NA	N	0	NA	120	80	81	174	70	NIL	NIL	NA	92	8.4	95	42	1.7	N
172	21 M	UM	MUSLIM	profession	21 N	0	NA	N	0	NA	122	82	83	171	65	NIL	NIL	NA	98	8.2	96	46	1.9	Y
173	21 M	UM	HINDU	profession	21 N	0	NA	N	0	NA	130	84	90	168	89	NIL	NIL	NA	80	8.8	98	40	1.8	N
174	20 M	UM	HINDU	profession	20 N	0	NA	N	0	NA	128	86	91	165	90	NIL	NIL	NA	82	9	96	46	2	N
175	20 M	UM	HINDU	student	20 N	0	NA	N	0	NA	120	78	80	168	70	NIL	NIL	NA	78	9.2	104	41	2.1	N

176	21	M	UM	HINDU	student	21	N	0	NA	N	0	NA	130	84	92	166	85	NIL	NIL	NA	88	7.6	96	42	2.2	N
177	21	M	UM	MUSLIM	student	21	N	0	NA	N	0	NA	124	80	78	170	72	NIL	NIL	NA	90	8.6	94	49	2.3	N
178	20	M	UM	MUSLIM	student	20	N	0	NA	N	0	NA	110	68	82	174	65	NIL	NIL	NA	92	8.8	93	44	2.3	N
179	23	M	UM	HINDU	student	20	N	0	NA	N	0	NA	118	70	86	168	67	NIL	NIL	NA	78	9.1	90	45	2.1	N
180	23	M	UM	HINDU	student	18	N	0	NA	N	0	NA	126	84	90	165	90	NIL	NIL	NA	80	8.5	93	42	2.1	Y
181	21	M	UM	HINDU	student	21	N	0	NA	N	0	NA	122	78	84	176	82	NIL	NIL	NA	89	8.8	96	40	1.6	N
182	21	M	UM	HINDU	student	21	N	0	NA	N	0	NA	126	80	88	166	72	NIL	NIL	NA	99	8.4	99	34	1.4	N
183	20	M	UM	CHRISCHIA	student	20	N	0	NA	N	0	NA	110	70	80	169	68	NIL	NIL	NA	80	8.2	101	49	1.3	N
184	20	M	UM	HINDU	profession	20	N	0	NA	N	0	NA	134	88	94	167	92	NIL	NIL	NA	92	8.8	95	40	1.6	N
185	21	M	UM	HINDU	student	21	N	0	NA	N	0	NA	140	90	96	165	90	NIL	NIL	NA	90	9	96	48	1.7	Y
186	21	M	UM	HINDU	student	21	N	0	NA	N	0	NA	134	88	92	165	88	NIL	NIL	NA	92	9.2	98	42	1.8	N
187	22	M	UM	MUSLIM	student	22	N	0	NA	N	0	NA	128	84	91	168	89	NIL	NIL	NA	94	7.6	96	46	1.8	N
188	21	M	UM	HINDU	student	21	N	0	NA	N	0	NA	126	86	90	169	85	NIL	NIL	NA	88	8.6	104	40	1.6	N
189	21	M	UM	HINDU	student	21	N	0	NA	N	0	NA	114	70	80	170	76	NIL	NIL	NA	90	8.8	96	46	1.9	N
190	21	M	UM	HINDU	student	21	N	0	NA	N	0	NA	120	70	84	174	71	NIL	NIL	NA	79	9.1	94	41	2.1	N
191	22	M	UM	CHRISCHIA	student	22	N	0	NA	N	0	NA	116	68	80	173	67	NIL	NIL	NA	85	8.5	93	42	2	N
192	23	M	M	CHRISCHIA	student	20	N	0	NA	N	0	NA	118	76	80	172	65	NIL	NIL	NA	83	8.8	90	49	2.1	N
193	22	M	UM	MUSLIM	student	22	N	0	NA	N	0	NA	124	80	82	175	69	NIL	NIL	NA	90	8.4	93	44	1.7	Y
194	21	M	UM	HINDU	student	21	N	0	NA	N	0	NA	128	88	90	168	90	NIL	NIL	NA	92	8.2	96	45	1.9	N
195	20	M	UM	HINDU	student	20	N	0	NA	N	0	NA	130	78	91	166	92	NIL	NIL	NA	86	8.8	99	42	1.8	N
196	20	M	UM	MUSLIM	student	20	N	0	NA	N	0	NA	134	84	94	166	93	NIL	NIL	NA	85	9	101	40	2	N
197	20	M	UM	HINDU	student	20	N	0	NA	N	0	NA	136	90	93	164	90	NIL	NIL	NA	90	9.2	95	34	2.1	N
198	21	M	UM	HINDU	profession	21	N	0	NA	N	0	NA	106	60	80	170	68	NIL	NIL	NA	95	7.6	96	49	2.2	Y
199	22	M	UM	HINDU	profession	22	N	0	NA	N	0	NA	114	60	78	170	65	NIL	NIL	NA	92	8.6	98	40	2.3	N
200	22	M	UM	HINDU	student	22	N	0	NA	N	0	NA	120	80	81	174	70	NIL	NIL	NA	98	8.8	96	48	2.3	N
201	23	M	UM	HINDU	student	19	N	0	NA	N	0	NA	122	82	83	171	65	NIL	NIL	NA	80	9.1	104	42	2.1	N
202	24	M	M	MUSLIM	student	19	N	0	NA	N	0	NA	130	84	90	168	89	NIL	NIL	NA	82	8.5	96	46	2.1	N
203	25	M	M	HINDU	profession	19	N	0	NA	N	0	NA	128	86	91	165	90	NIL	NIL	NA	78	8.8	94	40	1.6	N
204	21	M	UM	HINDU	profession	20	N	0	NA	N	0	NA	120	78	80	168	70	NIL	NIL	NA	88	8.4	93	46	1.4	N
205	22	M	UM	HINDU	profession	22	N	0	NA	N	0	NA	130	84	92	166	85	NIL	NIL	NA	90	8.2	90	41	1.3	N
206	21	M	UM	HINDU	profession	21	N	0	NA	N	0	NA	124	80	78	170	72	NIL	NIL	NA	92	8.8	93	42	1.6	Y
207	20	M	UM	HINDU	profession	20	N	0	NA	N	0	NA	110	68	82	174	65	NIL	NIL	NA	78	9	96	49	1.7	N
208	20	M	UM	CHRISCHIA	profession	20	N	0	NA	N	0	NA	118	70	86	168	67	NIL	NIL	NA	80	9.2	99	44	1.8	N
209	23	M	UM	HINDU	profession	19	N	0	NA	N	0	NA	126	84	90	165	90	NIL	NIL	NA	89	7.6	101	45	1.8	N
210	25	M	UM	HINDU	student	18	N	0	NA	N	0	NA	122	78	84	176	82	NIL	NIL	NA	99	8.6	95	42	1.6	N
211	21	M	UM	HINDU	student	21	N	0	NA	N	0	NA	126	80	88	166	72	NIL	NIL	NA	80	8.8	96	40	1.9	Y
212	22	M	UM	MUSLIM	student	22	N	0	NA	N	0	NA	110	70	80	169	68	NIL	NIL	NA	92	9.1	98	34	2.1	N
213	20	M	UM	HINDU	profession	20	N	0	NA	N	0	NA	134	88	94	167	92	NIL	NIL	NA	90	8.5	96	49	2	N
214	20	M	UM	HINDU	profession	20	N	0	NA	N	0	NA	140	90	96	165	90	NIL	NIL	NA	92	8.8	96	40	2.1	N
215	21	M	UM	HINDU	student	21	N	0	NA	N	0	NA	134	88	92	165	88	NIL	NIL	NA	94	8.4	96	48	1.7	N
216	20	M	UM	HINDU	student	20	N	0	NA	N	0	NA	128	84	91	168	89	NIL	NIL	NA	88	8.2	94	42	1.9	N

M: MARRIED
UM: UNMARRIED

BLUE COLC CASES
YELLOW CC CONTROLS

NA: NOT APPLICABLE